Case report

Adamantiades-Behçet's disease with inner ear involvement

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ABSTRACT

Adamantiades-Behçet's disease is a chronic recurrent inflammatory disorder involving the small and large vessels. Typical loci of manifestations are the mucous membranes, skin and eyes, as well as the joints and central nervous system. Other organs are not commonly involved. We present two patients, one with ocular and the other with mucocutaneous manifestation of Adamantiades-Behçet's disease. In addition, the first patient reported three episodes of sudden hearing loss while under immunosuppressive therapy for his eye involvement. The second, therapy-naive patient complained of tinnitus in his left ear. Careful examination revealed vestibular involvement in the first patient and retrocochlear involvement in the second. Inner ear involvement is an uncommon manifestation of Adamantiades-Behçet's disease. In case of relevant signs or history, such as hearing disturbance, tinnitus and/or vertigo, patients should be examined for inner ear involvement.

Introduction

Adamantiades-Behçet's disease is a systemic inflammatory disorder of unknown etiology, clinically characterized by relapsing oral and genital ulcers and ocular vasculitis. The original descriptions go back to 1931 and 1937 (1, 2). The disease exhibits a chronic recurrent and progressive character and may affect the small and large vessels in almost all organs (3). Involvement of the skin, eyes, joints, large vessels, gastrointestinal tract, central nervous system and genital system is common (4). In contrast, symptoms from the cardiopulmonary system, kidneys and ears are relatively rare. The first cases of inner ear involvement were described in 1980 by Brama and Fainaru (5), followed by further reports from several authors (6-9).

In this paper, we present two additional cases of Adamantiades-Behçet's disease with inner ear involvement and review the relevant literature.

Case reports

Case 1

A 25-year-old Turkish male presented after three episodes of sudden sensineural hearing loss during the last year at intervals of one and five months. Two episodes were unilateral involving the right ear (January and March) and one was bilateral (August). All episodes showed no signs of conductive hearing loss. There was a 5-year history of bilateral recurrent uveitis in both eyes as well as recurrent oral aphthae, disseminated skin papules and pustules, arthralgia and headache, but no claim of vertigo or a history of the use of autotoxic drugs.

A diagnosis of Adamantiades-Behçet's disease had already been made in 1994 in our Medical Center according to the "Classification and Regression Tree" criteria (10). There was no family history of Adamantiades-Behçet's disease or vestibulocochlear disorders. Since the time of the first diagnosis the patient had been under ophthalmological control and treatment with cyclosporin A (3 mg/kg body weight/d) and prednisolone (12.5 mg/d), which finally resulted in a stabilization of the disease with a slight improvement of the vision in his left eye from 0.02 sc to 0.05. His right eye vision of 0.4 sc remained stable over the entire period of treatment.

Interestingly, the episodes of hearing loss occurred despite the oral intake of immunosuppressives. No presence of oral aphthae was reported during that time, but arthralgia and occasionally headache were present.

Inner ear examination was performed by pure-tone audiometry, brainstem evoked response audiometry (BERA) and electronystagmography (ENG). In the acute stage of bilateral sudden hearing loss pure-tone audiometry revealed

sensineural hearing loss in the middle and high frequencies up to a maximum of 80 dB in the right ear and 70 dB in the left ear without signs of conductive hearing loss. After two vaers a residual bilateral senineural hearing loss of 25 dB at 4 kHz was could be observed. The patient had no history of exposure to noise. BERA and cerebral magnetic resonance imaging (MRI) showed no pathological results. After examination with Frenzel glasses, we suspected a hypoexcitability of the left peripheral vestibular organ, which was proved by ENG, performed with caloric, cervical and central stimulation tests. Caloric stimulation test (irrigation of the outer ear canal with water warmed to 30°C and 44°C) revealed clear hypoexcitability of the left vestibular organ. Considering the lack of dizziness, we interpreted these results as being an elder peripheral-vestibular lesion of the left ear with complete central compensation. The cervical and central tests showed no pathological findings.

Other diagnostic criteria such as the pathergy test, which was negative, and the HLA pattern with A2, A26(10), B21, B38(16), Bw4, Bw6 were inconspicious for the disease. Routine laboratory investigation showed blood cell counts, liver and renal function, c-reactive protein and a erythrocyte sedimentation rate (ESR) within normal limits, with slightly increased leukocyte numbers (12.2/nl). Antinuclear antibodies, complement 3 and 4 and total IgG levels in the serum were normal, while total IgM levels in the serum (9.1 U/ml) were slightly elevated (normal value < 6 U/ml).

Case 2

A 40-year-old Turkish male with a history of relapsing oral and genital aphthous ulcers since the age of 14 presented with tinnitus in his left ear and bilateral hearing impairment beginning 10 years ago. There was no history of inner ear noise damage or use of autotoxic drugs. He also reported arthralgias and occasional headache. Skeleton scintigraphy revealed severe inflammatory changes of the claviculosternal joints and the sternal part of the first ribs, as well as minor changes in the finger, hand and left knee joints. There was a history of pleural effusion of unknown etiology 2 years ago with no residuals. A diagnosis of Adamantiades-Behçet's disease was established according to the "Classification and Regression Tree" criteria (10).

There was a positive family history for Adamantiades-Behçet's disease based on his mother's recurrent oral aphthae and vision loss. Oral aphthae were also displayed by his uncle, 2 nephews and 1 niece. There was no family history of hearing loss.

Pure-tone audiometry revealed bilateral severe sensineural hearing impairment up to 65 dB in the high frequencies. Tinnitus could be detected at 4 kHz in the left ear. Impedance audiometry and stapedial reflexes showed normal results. BERA detected asymmetrical interpeak latencies J I to V with an elongation in the right ear (left ear: 4.4 ms and 4.25 ms at 70 and 80 dB; right ear: 4.6 ms and 4.65 ms at 70 and 80 dB). These results indicated a unilateral right retrocochlear hearing disturbance. MRI revealed no pathological findings. Examination with Frenzel glasses, ENG and a caloric stimulation test showed normal peripheral, cervical, central and vestibular functions. Eye examination showed a visual acuity of 1.0 in both eyes without any signs of acute or previous episodes of uveitis. The pathergy test was negative. The patient's HLA pattern was A2, A68(28), B 51(5), B 60(40), Bw 4, Bw 6, Cw 3. Laboratory investigation revealed no pathological findings in the blood cell counts, renal and liver function tests, c-reactive protein, anti-cardiolipin antibodies or antinuclear antibodies. The ESR was elevated at 46/54 mm (1st/2nd hour).

Discussion

Adamantiades-Behçet's disease has been occasionally associated with inner ear involvement, i.e. cochlear, retrocochlear and/or vestibular signs (Table I). These are rather rare and often overlooked complications of the disease and of other forms of systemic vasculi-

Table I. Review of the published cases with inner ear involvement distincted by cochlear, retrocochlear, vestibular or central vestibular tract lesions.

References	No. of cases	Cochlear (uni- or bilateral)	Retrocochlear	Vestibular	Central vestibular tract	Combination of cochlear and vestibular
Adler *et al*. (this report)	2		1			1
Belkahia *et al*. (7)	20	2		18		
Brama and Fainaru (5)	16	6	3	6		1
Elidan *et al*. (9)	28	28				
Gemignani *et al*. (6)	22	12		7	1	2
Igarashi *et al*. (11)	1	1 (endolymphatic hydrops)				
Narvaez *et al*. (12)	1	1				
Schwanitz *et al*. (13)	1	1				
Soylu *et al*. (8)	20	20				
Tsunoda *et al*. (14)	1	1				
Total	112	72	4	31	1	4
Percent	100%	64.3%	3.6%	27.7%	0.9%	3.6%

tis, such as systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, Wegener's granulomatosis, polyarteritis nodosa and giant cell arteriitis. Affected patients may report hearing loss, vertigo or tinnitus. Hearing loss at the higher frequencies may be hard to recognize for some patients, as it is marginal to the main speech area (13) and can occur in a slowly progressive hypoacusia.

Our first patient had recurrent acute hearing loss and showed a unilateral left peripheral vestibular lesion with complete central compensation. The second patient suffered from chronic unilateral tinnitus and hearing impairment of the high frequencies. In the BERA, he presented a retrochochlear disturbance on the right side while the lesion on the left was cochlear.

Different degrees of inner ear involvement in Adamantiades-Behçet's disease have been reported (7, 15). The findings in our second patient are compatible with the report of Brama and Fainaru (5), who reported retrochlear involvement in 16 patients. The symptoms began almost a decade after the initial manifestation of the disease. Ten patients had hearing disturbances, six had vertigo. Hearing loss was mostly bilateral with no preponderance for the high or low frequencies. Our patients developed inner ear involvement within approximately 5-15 years after the onset of the disease.

Like other manifestations of the disease, inner ear involvement has also been reported to be associated with HLA B 51 (6). HLA B 51 has been strongly suggested as a risk factor for severe eye and large vessel involvement, especially when combined with HLA A2 (4). This combination was present only in our second patient.

The first patient had three episodes of sudden hearing loss while undergoing immunosuppressive therapy with cyclosporin A and prednisolone. There was a residual unilateral hypoexcitability of the left peripheral vestibular organ which showed complete central compensation. Astonishingly, there was no history of vertigo. Therefore, it is likely that this symptom represented a slowly progressive inflammatory process.

It is not clear whether cyclosporin A itself is able to provoke episodes of sudden hearing loss. Sudden hearing loss under treatment with cyclosporin A has indeed been described in the literature only once in a renal transplantation patient (15). Administration of cyclosporin A and prednisolone in our patient over the last four years was not able to prevent hearing loss. Similar experiences have been reported by Soylu *et al.* (8) and Narváez *et al.* (12), who unsuccessfully treated 5 Adamantiades-Behçet's patients suffering from sudden cochlear hearing loss with cyclosporin A. On the other hand, Elidan *et al.* observed improvement of hearing with cyclosporin A treatment in 5 patients (9). The treatment of inner ear lesions is still unsatisfactory. Corticosteroids, vitamin B12,adenosinetriphosphate, nicotinic acid and inhalation of oxygen have been used successfully in one case (11). The combination of chlorambucil and corticosteroids led to improvement in another patient (13).

In conclusion, inner ear involvement should be taken into consideration in the systematic clinical examination of patients with Adamantiades-Behçet's disease. The cochlea seems to be more frequently involved than the retrocochlear tract, vestibular labyrinth or the central vestibular tracts. Retrocochlear or central vestibular deficits may hint at an involvement of the central nervous system, being the most severe symptom of the disease. Nevertheless, a drug history for ototoxic compounds should be carefully elucidated in each patient. Whether inner ear involvement is associated with unfavorable prognosis is still unclear and a specific therapy or prophylaxis for inner ear involvement is not known.

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