Behçet's disease – Clinical manifestations of twelve patients of an Autoimmune Disease Unit

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Abstract

The authors present a retrospective study of twelve patients with Behçet's disease (BD). All the patients met the criteria for diagnosis of BD (International Study Group for BD, 1990).

All the patients were Portuguese and Caucasian. Of the twelve patients, nine were female and three were male. The average age of onset of the BD was 31.3 years. All the patients presented recurrent oral ulcers, and 66.7% also had genital ulcers. Nine patients (75%) had ocular involvement. Dermatological manifestations were present in 58.3% of the patients. There was neurological involvement in 16.7% Osteoarticular manifestations were present in 75%. HLA was determined in all the patients; HLA-B51 was positive in two female patients. In seven patients there was a family history of recurrent oral ulcers, but just one with BD. The clinical evolution was marked by the development of amaurosis in one eye of a patient with panuveitis.

Key words: Behçet's disease, uveitis, oral ulcers, genital ulcers, erythema nodosum, vasculitis, cold sores.

INTRODUCTION

Behçet's disease (BD) was described for the first time in 1931, by a Greek Ophthalmologist, Adamantiades, who described a clinical case of a patient with hypopyon, orogenital ulcers, phlebitis and bilateral hydrarthrosis of the knees. In 1937, Hulûsi Behçet, a Turkish dermatologist, described the disorder as a trisymptomatic complex: characterized by recurrent cold sores, recurrent genital sores, and uveitis.

BD is a complex pathology which is characterized by a generalized vasculitis of the veins and arteries. The etiology remains unknown, but the most probably mechanism appears to be an excessive inflammatory response, triggered by exposure to an infectious agent (bacterial or viral) or environmental agent (chemical, metals, or others) in a genetically susceptible host. Although there is evidence to support the existence of environmental risk factors, epidemiological and family studies point to the existence of genetic risk factors. The existence of a genetic predisposition was seen in many of the families tested: the antigen HLA-B51, but this explains only around 19% of the total genetic predisposition. A recent study in 28 Turkish families with multiple cases of BD found evidence of a connection with risk of BD in chromosomes 6p22-24 (~13Mb telomeric to the site of HLA-B51) and 12p12-13 where various candidate genes are located. In Portugal, the positivity of HLA-B51 is around 60%.[1]

Although described worldwide, BD is more prevalent in Japan, the Middle East and the Mediterranean Basin, where it is classically known as "Silk Road Disease".[2] In these areas a more severe course is presented, this being the main cause of blindness due to uveitis.

It generally affects young adults, and the activity of the disease tends to decrease with age.

The diagnosis is exclusively clinical, and in view of the heterogeneity of the involvement of the organs and systems, the criteria for diagnosis used today were proposed in 1990, by the International Study Group for Behçet's Disease". The presence of recurrent oral ulcers is indispensible for diagnosis, and should be associated with at least two of the other criteria: genital ulcers, ocular lesions (inflammation of any ocular segment or of the veins of the retina), cutaneous lesions (erythema nodosum, pseudofolliculitis, papulopustules, etc) or positive pathergy test (appearance of papules or pustules around 48 hours after aseptic puncture of the skin).[3]

Besides the triad described by Hulûsi Behçet, other manifestations may also exist which are also diagnostic in nature. These include: cutaneous, joint (mechanical, inflammatory or mixed, with various locations and forms of expression), gastrointestinal, vascular (thrombophlebitis, thromboses or others)

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pulmonary, involvement of the central or peripheral nervous system, among others, as well as general signs and symptoms.

All the frequent manifestations of BD are self-limited, except for the ocular involvement. Repeated episodes of uveitis can lead to blindness.[4] BD is not a persistent and chronic inflammatory disease, but one that evolves through recurrent attacks of acute inflammation.[5]

The treatment of the disease consists mainly of control of inflammation and thrombosis. Multiple antiinflammatory and immunosuppressant drugs have been used, with some benefit.

The first case described in Portugal was in 1946 (Moreira Monteiro).[6] Several years afterwards, two further references appeared. Later on came various cases with Guerra Rodrigo and others, who did an excellent work of making DB known. Afterwards there came a national analysis, reaching an initial estimated prevalence of BD in Portugal of 1.3 patients per 100,000 inhabitants.[7]

In 1997, a national casuistic was carried out by the National Group for the Study of Behçet's disease, by Dr. Jorge Crespo. In this study, the prevalence of the disease was 2.4 per 100000 inhabitants, which is higher than previously described.[8]

The present study is a retrospective work with BD patients followed up at the Internal Medicine/ Autoimmune Disease Clinic of the Hospital São João, in Porto. The objective of our retrospective review was to characterize the clinical manifestations and evolution of patients with BD who met the current criteria for diagnosis.

MATERIALS AND METHODS

Twelve patients with diagnosis of BD were included in this retrospective study. All met the diagnostic criteria of the "International Study Group for Behçet's Disease": Indispensible presence of recurrent oral ulcers (>3/year) associated with another two of the four diagnostic criteria (genital ulcers, ocular lesions, cutaneous lesions and positive pathergy test).

All the patients were followed up by the Internal Medicine/Autoimmune Disease Clinic of the Hospital São João.

The following clinical manifestations were analyzed: age at onset of the symptoms, age on diagnosis, the presence of HLA B51, clinical evolution, and family history.

RESULTS

Of the twelve patients, nine (75%) were female and three (25%) were male. All the patients were Portuguese, and Caucasian. The average age on diagnosis was 31.3 years (the patients presented ages of between 15 and 60 years).

The time between the start of the first symptoms suggestive of BD and the fulfillment of the criteria for diagnosis of the disease was 4.4 years.

All the patients presented recurrent oral ulcers, which is necessary for diagnosis. The oral ulcers emerged as the first manifestation attributable to the disease in seven patients (58.3%), followed by ocular alterations in three patients (25%) and genital ulcers in two patients (16.7%) *(Table I)*.

All the patients presented recurrent oral ulcers (100%), while nine patients had ocular manifestations, eight had genital ulcers, eight had cutaneous involvement, two had neurological manifestations and nine had joint involvement. During our follow-up period, no patient presented pulmonary, renal, vascular, cardiac, or gastrointestinal manifestations, involvement of the peripheral nervous systems, or other manifestations *(Table II)*.

The recurrent oral ulcers present in all the patients, throughout their clinical evolution, and were generally painful, multiple and disappeared without leaving any scars. These ulcers were of classic location, in the oral mucosa, gums, oropharynx and tongue.

Genital ulcers were present in eight patients (66.7%), of which seven were female. These ulcers left a scar after disappearing.

Ocular involvement was observed in nine patients (75%) (six female and three male). The most frequent ocular manifestation was uveitis, present in six patients (50%), predominantly anterior. The presence of anterior uveitis was observed in four patients (33.3%); posterior uveitis in one patient, and panuveitis in one. Retinal vasculitis was documented in three patients (25%). The ocular impairment was bilateral in six patients (50%). There were important manifestations in these patients; one patient with panuveitis developed amaurosis in one eye. A marked decrease in visual acuity was observed in four patients *(Table III)*.

The most frequent cutaneous involvement was erythema nodosum, which was present in five patients (one man and four women). In two patients pseudofolliculitis could be seen (one female and another male). One patient presented erythema nodosum and

TABLE I

1st manifestation

1st manifestation	Nº of Patients	% Patients
Oral ulcers	7	58,3
Ocular	3	25,0
Genital ulcers	2	16,7

pseudofolliculitis simultaneously. In all, eight patients (66.7%) had cutaneous involvement.

Neurological involvement was present in two female patients: One with psychiatric disturbance (also followed-up at a psychiatric clinic and submitted to psychiatric treatment) and the other with headaches (study at the "Headache Consultancy" of the Hospital S. João, without any other explanation for the symptoms).

In relation to the undiagnosed manifestations, joint manifestations were present in nine patients (75%). Arthritis of the knees was present in two female patients: It was observed that arthralgias were more frequent in the knees, wrists and ankles, and were generally bilateral. The arthralgias were similarly divided between those of the inflammatory type and those of the mechanical type. One patient also had a diagnosis of ankylosing spondylitis HLA B27+, prior to the BD diagnosis.

The pathergy test was carried out in seven patients, and was considered positive in five.

The presence of HLA-B51 antigens was evaluated in all the patients, and was positive in two female patients (16.7%).

In this series of patients, seven had a family history of recurrent oral ulcers, but only one patient had a family member with diagnosis of BD (the mother), but this was not followed-up at our clinic.

TABLE II

Clinical manifestations

Clinical manifestations	Female gender	Male gender	% Patients
Oral ulcer	9	3	100,0
Genital ulcer	7	1	66,7
Ocular	6	3	75,0
Cutaneous	6	2	66,7
Neurological	2	0	16,7
Joint	7	2	75,0

TABLE III

Ocular manifestations

Ocular involvement	Female gender	Male gender	Total
Anterior uveitis	0	2	4
Posterior uveitis	2	1	1
Panuveitis	1	0	1
Retinal vasculitis	3	0	3

CONCLUSION

BD is a rare disease, but it exists. It is a disturbance of unknown etiology, which it is important to consider, particularly in situations of repeated uveitis with unknown cause, or when the complaints of repeated oral ulcers are associated with some other symptomatology.

Clinical experience confirms the multisystemic effects of BD, as well as the clinical variability that it can present.

This series, although small, has similar characteristics to those described in various published studies, except for the prevalence of females and the low percentage of HLA-B51+ (which was tested in all the patients).

The average age of diagnosis of BD was also in accordance with the international studies published (31.3 years).

During our 23-month follow-up, one patient with bilateral panuveitis suffered complete loss of vision in one eye, and there was a decrease in visual acuity in four patients. During this period, no patient needed to be hospitalized. Also, no deaths were recorded. ■

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