Behçet's disease: A profile of mucocutaneous features

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ABSTRACT

Background: Behçet's disease (BD) is a systemic inflammatory disease involving many systemic lesions characterized by vasculitis as a common basic pathologic process. Mucocutaneous (MC) features are considered as the diagnostic hallmarks.

Aim: To retrospectively determine the epidemiological and clinical aspects of BD mucocutaneous symptoms in Tunisia compared to those found in the literature.

Methods: Twenty-eight patients were involved in a single-center dermatological recruitment for a 27-year period (1980–2007) on the basis of international BD criteria.

Results: Our series included 19 males and 9 females. The mean age at onset was 28 years and the mean age at diagnosis was 37.9 years. The frequency of MC manifestations was as follows: oral ulcers (100%), genital ulcers (92.8%), other cutaneous signs (82.1%) such as papulopustular lesions (53.5%), and dermohypodermal nodes (11.53%), aphthous cutaneous ulcers (17.8%), and other lesions (leg ulcer: three cases, erythema multiform: one case, and infected pyodermatitis: one case). Systemic manifestations were present in 18 patients.

Conclusions: MC manifestations are hallmarks of the disease and usually the onset symptoms. The frequencies of the various MC signs seen in our study broadly match those found in the literature.

KEY WORDS

Behçet's disease, mucocutaneous symptoms

Introduction

Behçet's disease (BD) is a systemic inflammatory disease with unpredictable exacerbations and remissions. It involves many systemic lesions characterized by vasculitis as a common basic pathologic process (1). Mucocutaneous (MC) features may be considered the diagnostic hallmarks, making physical examination the most important step for the diagnosis because there is no pathognomonic test yet.

In this study, we sought to retrospectively determine the epidemiological and clinical aspects of BD mucocutaneous symptoms in Tunisia compared to those found in the literature and to evaluate the impact of the treatment and follow-up on the clinical severity of disease in our patients.

Methods

Twenty-eight patients were involved in this study. They were retrospectively recruited in our department over a 27-year period (1980–2007) on the basis of international BD criteria reported in 1990 (2; see Table 1).

The following was noted for each patient: epidemiological features (sex, age at onset, age at presentation, and diagnosis), significant familial medical history, MC features (aphthous oral ulcers [OUs], genital ulcers [GUs], papulopustular lesions [PPLs], erythema nodosum [EN], cutaneous ulcers, and other less common symptoms), results of the skin pathergy reaction when it was tested, visceral manifestations if present, treatment modalities, and outcome.

Results

Our series included 19 males (67.85%) and 9 females (32.15%), with a M:F ratio of about 2:1. The mean age at onset was 28 years (range 8–48). It was higher in females (34.1 vs. 30.6 years in men). The mean age at diagnosis was 37.9 years (range 19–62). The average duration between the onset symptom and the fulfillment of diagnostic criteria was calculated to be 6.18 years. A familial history of OUs was found in three patients, and coexistence of GUs in one case.

Recurrent aphthous OUs (see Fig. 1) were the most common manifestation (100%) followed by GUs (92.8%, see Fig. 2) and other cutaneous symptoms (82.1%) such as papulopustular lesions (53.5%, see Fig. 3), dermohypodermal nodes (11.53%), aphthous cutaneous ulcers (17.8%), and other lesions (leg ulcer: three cases, erythema multiform: one case, and infected pyodermatitis: one case). The severity of oral damage was determined in 11 patients; it was minor in 27.27% of cases, whereas ulcers took a herpetiform pattern in 72.7% of cases. The tongue was mainly affected (82.35%) while other sites of OUs were, in decreasing order: the lips (70.58%), cheek mucosa (47.05%), gingiva (11.76%), and palate (5.88%). However, the frequency of recurrence was identified in a few patients and then the figures could not be precise. Genital ulcers were noted in 16 patients and had almost the same prevalence in both sexes. Lesions were cicatricial in half the cases. Involvement was major in four patients, minor in three cases, and herpetiform in one patient. The location of GUs was precisely determined in 14 observations (10 M and 4 F). The scrotum was affected in 100% of men, and other affected sites were the penis (one case) and perineum (one case). The labia majora and minora were involved in 100% of women. Dermohypodermal nodes consisted of erythema nodosum (two cases) and superficial phlebitis (one case). The skin pathergy reaction, tested in 16 patients (57.1%), was positive in 50% of cases. Systemic features were present in 18 patients and are summarized in Table 1.

In 10 patients, local treatment using antiseptic, anti-inflammatory, and anesthetic mouthwashes was prescribed. Twenty-four patients were treated with colchicine with a good safety profile. Oral steroids were used in four patients. Thalidomide was used in only two patients after failure of treatment with colchicine and steroids. In two cases, severe visceral symptoms (neuro-ophthalmological and neuro-vascular) required intravenous administration of steroids with immunosuppressive therapy (cyclophosphamide and azathioprine). Other systemic therapies such as

Table 1. International study group criteria for the diagnosis of Behçet's disease (2).

Criterion	Description
Recurrent oral ulceration	Minor, aphthous, major aphthous, or herpetiform ulceration observed by physician or patient that recurred at least 3 times in one 12-month period
Plus 2 of the following criteria:	
Recurrent genital ulceration	Aphthous ulceration or scarring observed by physician or patient
Eye lesions	Anterior uveitis, posterior uveitis, or cells in vitreous on slit lamp examination; or retinal vasculitis observed by ophthalmologist
Cutaneous lesions	Erythema nodosum, pseudofolliculitis, or papulopustular lesions; or acneiform nodules observed by physician in post-adolescent patients not receiving corticosteroid treatment
Positive pathergy test	Read by physician at 24 to 48 hours

Note: Findings applicable only in the absence of other clinical explanations.

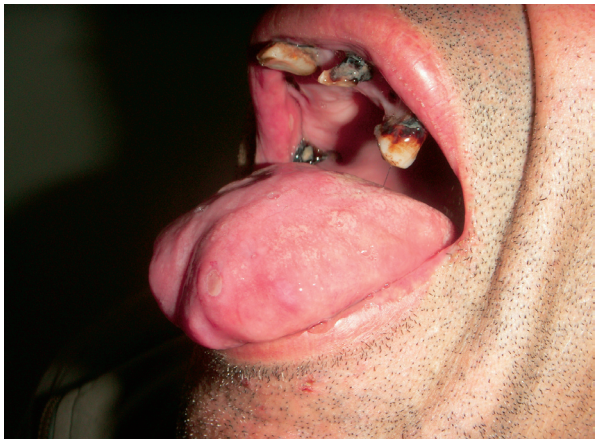

Figure 1. Oral ulcer on the lateral side of the tongue with rolled borders and yellow necrotic base.

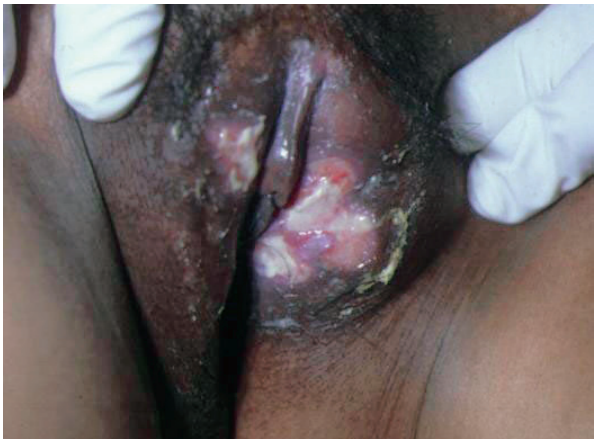

Figure 2. Genital ulcer in female patient.

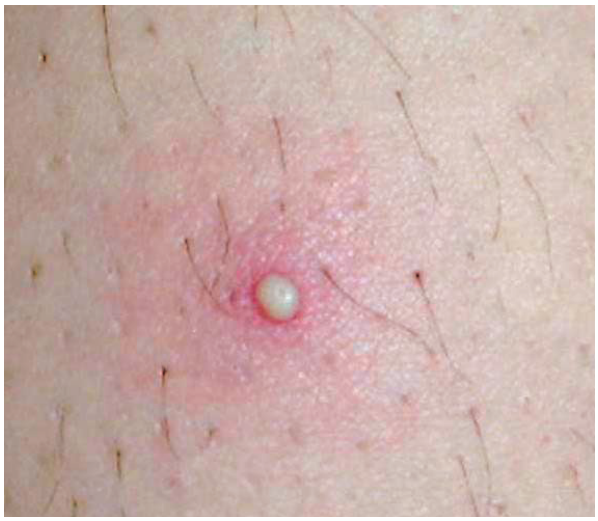

Figure 3. Papulopustular lesions.

pentoxifylline and dapsone were indicated in severe forms. The outcome was favorable, with rapid and complete healing of the ulcers within a few days in 89.2% of cases. No side effects were noted. One patient suffered from a physical as well as intellectual impact with a speech impediment due to OUs. Another patient later developed a lower vena cava thrombosis. Recurrence of MC signs was noted in five patients and one patient developed perivasculitis. Four patients left the study.

Conclusions

We report a series of Tunisian BD from a single-center dermatological recruitment. BD is endemic in the Mediterranean basin. In our department, its prevalence was estimated at almost one case/year.

Because of the lack of a universally recognized pathognomonic laboratory test, BD diagnosis is primarily based on clinical criteria (3). Our study has shown that MC lesions are the most common manifestations in BD. The high frequency of these symptoms at any time in the course of the disease, especially as onset symptoms, confirms their importance for the diagnosis (4, 5) as given in the new, internationally agreed-upon (6) set of diagnostic criteria established by the International Study Group for Behçet's Disease (2), which rely heavily on MC manifestations.

The frequencies of the various MC symptoms seen in our study broadly match those found in the literature (3, 7, 8, 9, 10), in which their occurrence takes place in the following decreasing order: OUs, GUs, PPLs, and EN; see Table 2. It is notable that only the skin pathergy test varies widely between series (11) because it depends on ethnic factors of the populations studied as well as on the technique diversity and test interpretation (8).

Among visceral signs of BD, ocular involvement was the most common manifestation in our series, followed by articular symptoms, neurological involvement, and vascular symptoms. Concerning systemic lesions, results are discordant in the literature (Table 3) even though overall, ocular, and articular involvements remain the most frequently reported.

Our study, in agreement with another Tunisian series (9) and reports from Turkey (12) and Iran (10), noted a male predominance. In contrast to this predominance in Arab countries, other authors reported a roughly equal sex distribution in western populations (3). It is noteworthy that the profile of BD in Tunisia and other Mediterranean areas characterized by predominance in males and a younger age at onset are associated with more severe disease (3, 7). BD usually occurs around the third decade of life. However,

Table 2. Frequencies of systemic manifestations of BD in our study.

Systemic manifestations	Number of cases	Frequency (%)
Ocular involvement (OI)	8	28.57
Neurological involvement (NI)	8	28.57
Vascular involvement (VI)	6	21.42
Articular involvement (AI)	5	17.85

the disease is often diagnosed with a delay of several years after onset, as it was the case in our study, usually because of the benign nature of the onset symptoms, which leads to misdiagnosis. In fact, it has been noted that the duration between the time point of fulfillment of diagnostic criteria and the diagnosis itself tended to be longer in patients that had only MC lesions than in patients that had serious organ involvement (7). Therefore, familiarity with the MC spectrum of BD is imperative for prompt diagnosis and prevention of severe systemic manifestations. In addition, patients with recurrent OUs should be regularly followed, especially in the Mediterranean regions.

Treatment of BD remains challenging. In spite of the wide spectrum of therapeutic agents, none of them is curative and no standard therapy has yet been established for the disease. Moreover, available therapeutics act with varying success and some of them are associated with significant side effects. The choice of treatment is based on the severity of clinical manifestations. Colchicine is considered a good alternative for improvement and prevention of MC symptoms. In our patients, it was widely associated with topical application in mild forms of BD. We usually used 0.5 to 2 mg per day. How long should one wait for a response? Is this continued for years or is the medication discontinued after a certain period?

Al-Waiz et al. found that the combination of colchicine and benzathine penicillin appears to be of greater efficacy in the treatment of Behçet disease than the use of either drug alone (13). In severe forms, additional systemic therapies are necessary, such as oral corticosteroids, azathioprine, dapsone, cyclophosphamide, pentoxifylline, thalidomide, and anti-TNFα (14).

In conclusion, despite the small sample of patients with BD recruited in one dermatological department, this study confirms that MC manifestations are hallmarks of the disease and usually the onset symptoms. Because a high incidence of vital organ involvement has been reported in BD, close monitoring and continuous surveillance is warranted, especially in young male patients.

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