

Assessment of Different Manifestations of Known Cases of Behçet's Disease

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ABSTRACT

Background & Objective: Behçet's disease (BD) is a multisystemic inflammatory vascular disorder with an autoimmune background. It is a genetic disease which can be affected by environmental factors. Behçet's disease may involve different organs like urogenital system, skin, eyes, and gastrointestinal system. The prevalence of the disease varies considering the geographic area and genetic predisposition. This study aims to evaluate some clinical features of mucocutaneous lesions of BD.

Materials & Methods: This cross-sectional study was done on 43 patients with BD (24 men, 19 women). Age, sex, disease duration, and history of receiving medication were investigated. The self-reported questionnaire was completed by participants. Skin manifestations and genital and ocular involvements were also documented.

Results: Male to female ratio was measured 1.26:1. Oral aphthous commonly localized on the lips. Ocular involvements and skin lesions prevalence percentages were 76% and 48%, respectively. There was a statically significant correlation between ocular lesions and age. Skin lesions and the frequency of oral aphthous per year had a significant relationship. There also was a significant relationship between the incidence of ocular lesions and skin lesions.

Conclusion: Oral aphthous, the most popular manifestation of BD, is the hallmark of diagnosis. Thus, patients with oral aphthous require close surveillance for other manifestations of BD for timely diagnosis and reference to a rheumatologist.

Keywords: Aphthous, Behçets syndrome, Eye manifestations, Genitalia, Skin manifestations, Stomatitis.



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Introduction

Behçet's disease (BD) is a chronic vascular immune-mediated disease. The etiology of the disease is not completely recognized (1-8). BD can be found anywhere throughout the world; however, it is more prevalent in countries along the ancient Silk Road such as Turkey, Iran, Iraq, and Japan. The pattern of BD depends on race (1, 3, 4). Initially published in 1937, BD criteria included triad signs: recurrent oral aphthous, genital ulcer, and ocular involvement (1-3, 6, 9-11). Strong association of BD with HLA-B51 has been confirmed in many different ethnic groups from the Middle East to the Far East, and about 40–80% of mentioned patients possess HLA-B5 or B51 (12-16).

BD is a multisystemic disease with prominent manifestation of oral aphthous. This finding usually appears as the first symptom, followed by genital ulcers, skin lesions and ocular involvement (1-8).

Sometimes, BD is accompanied by arthralgia, arthritis, intestinal ulceration and CNS complications (1).

The most recent international criteria for BD were approved in 2006 in which scoring four points or more was strongly suggestive of BD. Each of oral, ocular and genital ulcers were allocated two points while skin lesions, neurologic, and vascular manifestations had a score of one. Despite being optional, a positive pathergy test also has a score of one (6, 8).

According to the recent criteria, oral aphthous ulcers are considered the main components of the disease (1-4, 10, 17-20). The first BD symptom is usually observed when patients are in their 30s or 40s. The sooner the disease begins, the more severe the disease will be, and the longer it will take to recover (1-4, 6, 10, 18-22). Behçet's disease manifestation differs between races and sexes (1, 5, 23, 24). In Middle East, men are more susceptible in contrast to Japan and Korea (1, 2, 25-27).

Materials and Methods

A total of 43 consecutive BD patients composed of 24 males and 19 females took part in this study. They

were followed at a private rheumatologic clinic and met the inclusion criteria. They were included in the study from July to November 2018. All patients agreed to participate in the study and signed a letter of informed consent. After gathering a comprehensive history, participants' data were collected. Mentioned data included patients' age, sex, disease duration, and history of receiving medication. The questionnaires were completed by the participants themselves. They were asked about the clinical characteristics of the disease (number, location, and size of oral ulcers). Skin manifestations and genital and ocular involvement were also documented. After filling out the questionnaire, an oral examination was performed by a trained senior dentistry student to determine each participant's oral health status.

The inclusion criteria were as follows: Regular visits by the related specialist, having a complete medical document, and disease duration of more than one year. Patients with poor oral hygiene, tobacco use, or a simultaneous disease with a probable manifestation of aphthous ulcers (e.g. anemia, celiac, or inflammatory bowel disease) were excluded from the study.

Our study was approved by the ethics committee of Yazd Shahid Sadoughi University of medical sciences (IR.SSU.REC.13970037).

The obtained data were analyzed using SPSS 17. The chi-square and Fisher exact tests were used. Differences were defined as statistically significant at $P < 0.05$.



Figure 1. Oral and labial manifestations of BD patients



Figure 2. Skin involvement in BD patient



Figure 3. Eye involvement in BD patient

Results

Men accounted for 24 of the 43 study patients, and women accounted for 19. The male to female ratio was determined to be 1.26:1. Patients' ages ranged from 19 to 64 years. BD was mostly prevalent among the 40-49 age group (39.5%) and least common in participants who were under 30 (4.7%). Oral aphthous were evident in 100% of patients. They were commonly localized on the lips (46.5%) and buccal mucosa (37.2%). It

occurred two to five times per year in 16 patients (37.2%), less than twice per year in 16 patients (37.2%), and more than five times per year in 11 patients (25.6%). When family history was evaluated, six (13.9%) patients had a positive history of BD in their family, and the others had either a negative or an unknown history. Previous genital ulcers were determined in 28 patients (65%). Ocular involvement and skin lesions were reported in 76% and 48% of the patients, respectively ([Table 1](#)).

Table 1. Some clinical features of the patients with BD

Variable data	classification	number	%
Duration of disease	<1 year	0	0
	1-5 year	1	2.3
	>5 year	42	97.7
Familial history	yes	6	14
	no	37	86
Incidence of oral aphthous lesion per year	<2	16	37.2
	2-5	16	37.2
	>5	11	25.6
location	Lip	20	46.5
	Sublingual	6	14
	Floor of mouth	1	2.3
	cheek	16	37.2
Genital involvement	Yes	28	65.1
	No	15	34.9
Ocular involvement	Yes	33	76.7
	No	10	23.3
Skin involvement	Yes	21	48.8
	No	22	51.2

There was a statistically significant relationship between skin lesions and the incidence of oral aphthous ulcers per year ($P=0.049$) (Table 2) (Figures 1 and 2).

Patients with more frequent oral aphthous had more skin lesions. Also, ocular involvement tended to occur

more frequently in patients older than 50 years ($P=0.038$). More than half of the patients dealt with ocular and genital involvements (76% and 65%, respectively). Skin lesions were observed in 21 patients (48.8%) (Table 3).

Table 2. Correlation between skin involvement and frequency of oral aphthous per year

frequency of oral aphthous per year	Skin involvement	
	Yes N (%)	No N (%)
<2	6(37.5)	10(62.5)
2-5	6(37.5)	10(62.5)
>5	9(81.8)	2(18.2)

Table 3. Correlation between clinical manifestations and age

age manifestations		<30	30-39	40-49	>50	P value
		N (%)	N (%)	N (%)	N (%)	
ocular	Yes	1(50)	7(58.3)	14(82.4)	11(91.7)	0.038
	No	1(50)	5(41.7)	3(17.6)	1(8.3)	
skin	Yes	1(50)	5(41.7)	9(52.9)	6(50)	0.961
	No	1(50)	7(58.3)	8(47.1)	6(50)	
genital	Yes	1(50)	10(83.3)	11(64.7)	6(50)	0.367
	no	1(50)	2(16.7)	6(35.3)	6(50)	

Table 4. Correlation between skin lesions and ocular involvement.

Ocular involvement	Skin involvement		Total N (%)
	Yes N (%)	No N (%)	
Yes	13(39.4)	20(60.6)	33(100)
No	8(80)	2(20)	10(100)

Frequency of skin lesions and genital involvement did not increase with age.

Even though there was no statistically significant relationship between skin lesions and genital involvement, the relationship between ocular involvement and skin lesions was significant. ($P=0.034$) (Table 4).

Discussion

Many studies have been conducted about the clinical features of BD in different countries. Due to the potent role of genetics, its manifestation could vary across different geographic areas and ethnic groups.

Therefore, occasional evaluation of BD characteristics is of great importance even in the same country. Although the small sample size of this study was one of its limitations, the strict inclusion criteria were applied to increase its accuracy. In this cross-sectional study, the occurrence of some clinical manifestations of BD was evaluated in an Iranian population. Despite the limited population, this study is valuable since no previous study has examined the clinical features of BD in Yazd from a comprehensive point of view.

A notable advantage in the present study was ruling out systemic diseases related to oral aphthous. This led to more reliable results in comparison with previous studies. The male to female ratio was 1.26/1. The predilection for male involvement is similar to reports

by Davari (9) and Lennokove (23) but different than California, US-based studies (28, 29).

Regarding the inclusion criteria, BD patients with a disease duration of at least one year were included in the study. Oral aphthous ulcers were seen in 100% of patients, indicating that this is a hallmark of BD, independent of patient demographics. It occurred more than five times per year in 25.6% of patients. The importance of family history is supported in the literature (23). The occurrence frequency of oral aphthous in the families was 14%. This is close to the proportion detected in the analysis of Ugurlu *et al.* (30); however, this percentage is lower than the percentages reported in some previous studies (31, 32). This low percentage may be due to the lack of knowledge about family involvement among some patients.

Some studies ignored the location of oral aphthous ulcers (1, 23, 31). In this study, oral aphthous was mostly seen on the lips, followed by buccal mucosa and tongue, respectively. This finding was in accordance with the results of Alposy (2) and Cansu (31), who stated that the tongue was the most common involved location (31).

Genital ulcers were found in 28 patients (65.1%). These results are in line with studies by Davatchi and Sula (1, 33), who reported involvement rates of 64.4% in Iran and 70% in Turkey. These percentages are less than what Lennikovs reported in Russia (23). These differences could be attributed to special HLA in some races. It is worth mentioning that the results may be underestimated due to the shame, fear, or disregard of patients (33).

The frequency of ocular involvement in this study was 76.7%. This ratio was higher than what was reported in previous studies in Iran and Turkey (1, 33). This may be attributed to the warm and dry weather of geographic area of the study. Another reason could be the higher incidence of ocular involvement in men in this study (5). This finding is consistent with the Sula's findings, who reported the disease to be more common in males and young patients (33).

Many of our patients were referred by ophthalmologists, and they were diagnosed based on ocular involvement in the advanced stage of BD. There was a statistically significant relationship between age and ocular involvement. Ocular involvement would increase with aging (33). Regarding the high frequency of ocular involvement in the BD patients, ophthalmologic consultations should be considered annually. These results indicated that the frequency of oral aphthous can be used as a severity index for BD. This was concluded because of the significant relationship between skin lesions and the frequency of oral aphthous per year. The more severe the disease, the higher the possibility of involvement of organs in the course of the disease.

Conclusion

Oral aphthous, the most widespread manifestation of BD, is the hallmark of BD diagnosis. Thus, patients with oral aphthous require close surveillance for other manifestations of BD. Timely diagnosis and reference to Rheumatologists improves patients' quality of life. Ocular lesions can be affected by age. There was a positive association between skin lesions and ocular involvement.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of Interest

Authors declared no conflict of interest.

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