BEHCET'S DISEASE: AN ASSESSMENT OF CUTANEOUS, OCULAR AND ARTICULAR CHARACTERISTICS IN THE SOUTH OF JORDAN

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ABSTRACT

Objective: To determine the spectrum and the frequency of skin, eye and joint manifestation in patients with Behcet's Disease in the southern parts of Jordan.

Methods: Twenty three patients diagnosed to have Behcet's Disease were included in the study. The diagnosis was based on the criteria proposed by the International Study Group of Behcet's Disease. In order to detect the various cutaneous, ocular and articular manifestations of the disease, all patients were thoroughly evaluated by a dermatologist, an ophthalmologist, and a rheumatologist. Pathergy test was performed for all patients.

Results: Fifteen patients were males (65.1%) and eight were females (34.8%). The mean age was 32.5 years. Oral ulcers were detected in all the patients and genital ulcers were found in 56.5% of the patients. Other skin lesions were detected in 56.5% of the patients. Ocular lesions occurred in 60.8% of the patients. Joint involvement was found in 43.4% of the patients.

Conclusion: The pattern of cutaneous, ophthalmic and articular manifestation in our group of patients was different from patterns reported in countries with different races and similar to patterns in neighboring countries. The results may reflect the effect of differences in both the genetic background and environmental factors among different countries.

Key words: Articular, Behcet's disease, Cutaneous, Ocular.

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Introduction

Behcet's disease (BD) is a chronic inflammatory disorder affecting multiple organ systems in the body with an unpredictable course of exacerbations and remission.[1] BD has a spectrum of manifestations that includes skin and mucus membrane lesions, ocular inflammation, arthropathy and less frequent manifestations of other organ involvement.[1,2] Both genders are affected, mainly those in the age group of 20 to 50 years.[1] The disease occurs worldwide, however it has a higher incidence in the Far East, Middle East and the countries around the Mediterranean.[1,3] Since vascular manifestations are common in BD, it is considered as systemic vasculitis.[3,4]

The exact etiology of the disease is not known.[1] A number of infectious agents, immune mechanisms and genetic factors have been related to occurrence of BD.[1,3] The role of HLA-B*51 gene has been confirmed recently, although its contribution to the overall genetic susceptibility of BD was estimated to

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Table I. International Classification Criteria of Behcet's Disease [5]

- In the absence of other clinical explanation, patients must have:
  Recurrent oral ulceration (aphthous or herpitiform) observed by the physician or patient recurring at least three times in a 12-month period.
- And two of the following clinical signs:

1. Recurrent genital ulceration.
2. Eye lesions: anterior uveitis, posterior uveitis, cells in the vitreous humor by slit lamp examination or retinal vasculitis observed by an ophthalmologist.
3. Skin lesions: erythema nodosum, pseudofolliculitis, papulopustular lesions or acneiform nodules in adult patient without corticosteroid therapy.
4. Pathergy test read by a physician at 24-48 hours.

be only 19%.[3] T-cell activation with production of a variety of cytokines has been showed to play a pivotal role in the pathogenesis of this disease.[3]

This study was conducted to characterize the spectrum of cutaneous, ocular and articular manifestations of BD in the out patient clinics in two hospitals in the southern area of Jordan.

Methods

This study was conducted during the period from August 2001 through July 2004 in two tertiary hospitals in the southern area of Jordan: Prince Ali Bin Al-Hussein and Prince Zeid Bin Al-Hussein Hospitals. Diagnosis of BD was based on the criteria proposed by the International Study Group for Behcet's Disease[5] (Table I). We included new and old cases of patients who fulfilled the criteria for the diagnosis. All patients were examined by a dermatologist carefully. Patients were asked about the presence of any skin symptoms and/or lesions. The whole skin and mucus membranes were fully examined. The presence of any cutaneous lesion was recorded. A Pathergy test was performed and read by a dermatologist for all patients. The amount of 0.2 ml of normal saline was injected interadermally on the flexor aspect of the forearm using a 22 gauge needle, and the site was evaluated after 24 to 48 hours. The presence of a sterile pustule with erythematous rim or indurated erythema of at least 0.5 cm was considered as a positive test.

Eye assessment was conducted by an ophthalmologist. Detailed ophthalmic history was obtained for all patients. A complete ocular examination was performed for all patients as well, including visual acuity by Snellen chart; slit lamp biomicroscopy for anterior segment assessment, tonometry by Goldman applanation tonometer, fundus examination by +90 D lens and indirect ophthalmoloscopy. All findings were recorded.

All patients were examined thoroughly by a rheumatologist. A standard detailed history was taken for each patient, especially the presence of arthralgia and morning stiffness. All joints were examined for the presence of signs of arthritis. Radiological investigations were conducted whenever appropriate. Inclusion of data on inflammatory markers were not presented in this study because these tests are not available in Southern military hospitals in Jordan.

Results

Out of the twenty three patients 15 (65.1%) were male and eight (34.8%) were female with approximately 2:1 male to female ratio. The mean age was 32.5 years and the range was from 20-50 years. The distribution of patients according to their age and gender and the clinical features of BD among our patients are summarized in Table II. Oral ulcers were detected in all patients and genital ulcers were found in 56.5% of patients. Cutaneous lesions were detected in 56.5% of patients. Pathergy test was positive in 47.8%. Ocular involvement was seen in 60.8% of patients. Uveitis was the most common ocular finding (30.4%) followed by cataract formation (13.0%) and glaucoma (4.3%). Articular manifestations were seen in 43.4% of patients and included arthritis in 21.7% (5/23). Frequencies of joint involvement are illustrated in Table II.

Discussion

BD has been studied in different countries. The type of manifestations was essentially the same, although the frequencies of different manifestations varied greatly. Table III illustrates the spectrum of BD manifestations from worldwide reports. The male-to-female ratios in BD patients have varied in different reports. In our study, the male to female ratio was 2:1 which is similar to the ratio (2.3:1) reported in the Northern area of Jordan.[6] A male predominance has been also reported in neighboring Arab countries. For example the ratio was found to be 3.4:1 in Saudi Arabia,[7] 3.1:1 in Kuwait,[8] 11:1 in Lebanon[1] and 5.3:1 in Egypt.[1] In contrast, female predominance was a consistent finding in reports from Far East countries. Ratios of 1:1.4,[9] 1:1.75[10] and 0.63:1[11] have been reported from Korea.

Table II. Distribution of patients according to age and gender, clinical features, cutaneous manifestations, eye lesions and articular manifestations

Age (Year)	Male (n=15) Number (%)	Female (n=8) Number (%)	Total (n=23) Number (%)
≤ 20	1 (4.3)	1 (4.3)	2 (8.7)
21-30	7 (30.4)	4 (17.4)	11(47.8)
31-40	5 (21.7)	2 (8.7)	7 (30.4)
41-50	2 (8.7)	1 (4.3)	3 (13.0)
>50	0 (0)	0 (0.0)	0 (0)
Total (%)	15 (65.1)	8 (34.8)	23 (100)
Clinical criteria			
Major			
Oral ulcer	15 (100)	8(100)	23 (100)
Genital ulcer	10 (66.7)	3 (37.5)	13 (56.5)
Skin lesion	8 (53.3)	5 (62.5)	13 (56.5)
Eye lesion	10 (66.7)	4 (50.0)	14 (60.8)
Minor			
Articular	6 (40)	4 (50)	10 (43.4)
Gastrointestinal	1 (6.6)	1 (12.5)	2 (8.6)
Vascular	2 (13.3)	0 (0.0)	2 (8.6)
Neurological	1 (6.6)	0 (0.0)	1 (4.3)
Pathergy reaction	7 (46.6)	4 (50.0)	11(47.8)
Skin Lesions			
Folliculitis	6 (40.0)	2 (25.5)	8 (34.7)
Erythema nodosum-like lesions	4 (26.7)	3 (37.5)	7 (30.4)
Acneiform eruption	2 (13.3)	2 (25.0)	4 (17.4)
Furuncle	1 (6.6)	2 (25.0)	3 (13.0)
Abscess	1 (6.6)	1 (12.5)	2 (8.6)
Thrombophlebitis	0 (0.0)	1 (12.5)	1 (4.3)
Eye lesions			
Uveitis	5 (33.3)	2 (25)	7 (30.4)
Cataract	2 (13.3)	1 (12.5)	3 (13.0)
Glaucoma	1 (6.7)	0 (0.0)	1 (4.3)
Retinal hemorrhage	1 (6.7)	1 (12.5)	2 (8.6)
Retinal detachment	1 (6.7)	0 (0.0)	1 (4.3)
Total	10 (66.7)	4 (50.0)	14 (62.9)
Articular Manifestation			
Artharlgia	2 (13.3)	2 (25.0)	4 (17.4)
Monoarthritis	1 (6.6)	1 (12.5)	2 (8.7)
Polyarthritis	1 (6.6)	1 (12.5)	2 (8.7)
Oligoarthritis	1(6.6)	0 (0.0)	1 (4.3)
Sacroilitis	1 (6.6)	0 (0.0)	1 (4.3)
Total	4 (39.7)	4 (50.0)	10 (43.4)

Table III. The spectrum of BD manifestations in worldwide reports

Country	M:F Ratio	Mean Age	OU* %	GU** %	Skin lesions %	Ocular Disease %	Joint Disease %
Germany[2]	1:1	25	99	75	76	59	59
Turkey[14]	1.03:1	25.6	100	88.2	-	28.9	15.9
Korea[9]	1:1.4	29.3	99.2	88.4	73.4	39.5	31.2
Singapore[13]	1:1.1	32.7	100	64.9	48.6	35.1	56.8
Taiwan[16]	-	35.7	100	55	90.9	55	31.8
China[12]	1:1.1	36.2	100	81	73	35	54
Iran[19]	1.19:1	26	96.8	65.3	69.3	55.6	34.3
Lebanon[15]	-	-	95	78	-	-	65
Jordan[6]	2.3:1	-	100	65	35	65	55
Saudi Arabia[7]	3.4:1	29.3	100	87	57	65	37
Kuwait[8]	3.1:1	-	100	93	76	69	69
Australia[18]	-	-	90	68	84	66	78
Japan[17]	-	-	98.2	73	87	69	57
Iraq[17]	-	-	97	83	75	48	48

*Oral Ulceration **Genital Ulceration

Table IV. Reported cutaneous manifestations of BD

Country	EN* %	Folliculitis %	Acneiform %	Furuncle %	Thrombophlebitis %	Ulceration %	Abscess %
Germany[2]	37	50.8	-	21.5	14.1	9.9	-
Turkey[6]	47.6	-	54.2	-	-	-	-
Korea[7]	62.1	-	56.8	-	2.3	2.3	-
Singapore[8]	40.5	-	32.4	-	-	-	-
Taiwan[9]	64	-	27	-	-	-	-
Korea[10]	55.3	25.3	10.9	6	2.6	2	1.4
China[12]	74	44	30	-	-	-	-
Iran[14]	22.2	60.6	-	-	-	-	-

* Erythema nodosum

In China and Singapore the M:F ratio was found to be 1:1.1.[12,13]

The fact that male predominance was noted in our study and in nearby Arabic countries suggests that genetic factors may have a role in the expression of the disease. Social and religious factors may also have influenced the difference as well.

The prevalence of recurrent oral ulcers, which was a major diagnostic criterion for BD among our patients, was 100%. In most series, this manifestation is present during the course of the disease in nearly all patients (Table II). This may be attributed to the fact that oral ulcerations are painful and arise in area that is easily recognized by both the patient and the physician. In contrast, the prevalence of genital ulcers (56.5%) was lower than prevalence rates reported in similar studies. In the Northern area of Jordan the prevalence rate of genital ulceration was 65%, in Turkey 88.2%,[14] in Korea 82.4%,[9] in Lebanon 78%,[15] in Saudi Arabia 78%[7] and in Kuwait 93%.[8] Patients may under report this important manifestation of the disease for many reasons. Firstly, there may be a lack of awareness that these ulcerations are part of their disease and are an important sign which needs to be reported to their treating physician. Secondly, some patients were not able to recognize the ulcers and they attributed the pain they feel to something else. This is particularly true in female patients where genital ulceration can occur in a hidden area. Thirdly, the cultural background of the patients where people, especially females, are unwilling to expose the genital area for a clinical examination may have contributed further for this low prevalence rate of genital ulcerations in our group of patients.

A variety of skin lesions has been reported in association with BD. This study noted that 56.5% of patients had a cutaneous manifestation. Strikingly, in the Northern area of Jordan, the occurrence of skin manifestation has been reported to be 35%[6] which is much lower than our finding. This may be a result of the difference in climate between the two areas. In addition, all our patients were examined thoroughly by a dermatologist with great care and all types of skin lesions were recorded. This may have contributed to the detection of more skin lesions resulting in a higher prevalence rate in our group of patients from the Southern area of Jordan than those from Northern areas. However, both prevalence rates of skin lesions are still lower than rates reported in most countries like Taiwan (90.9%),[16] Japan (87%),[17] Korea (84.3%)[10], Australia (84%)[18] and Germany (76%),[2] (Table III).

The finding of lower rates of cutaneous manifestations in Jordan may be due to the variation in the genetic expression of the disease among different races and influence of different environmental factors. This may be supported by the fact that an approximately similar rate of skin involvement (57%) has been reported in Saudi Arabia; a neighboring country in which population is more likely to share a common genetic background with Jordanians.[7] The most common cutaneous manifestations were folliculitis (34.7%), erythema nodosum-like eruption (23.4%) and acneiform eruption (17.4%). There are many reports on cutaneous manifestations of BD (Table IV) and although there is variation of the frequency of skin lesions, the type of most frequent lesions are the same. Difference in ethnic background and geographical distribution is an important factor that may contribute to this variation. The fact that most reports, like ours, were conducted on a small number of patients may have contributed to statistical bias and a consequent variation of the frequency of the various skin manifestations.

Pathergy test represents a non specific skin hyper-reactivity induced by intradermal needle prick. The prevalence of a positive Pathergy test among our patients was 47.8%. The positivity rates of the test are especially high in Middle East countries. The prevalence of positive Pathergy test in Turkey was 56.8%, [14] in Iran 57.4% [19] and in Kuwait 34%.[8] In contrast, a low rate of positive reactions has been reported from Korea 15.4%,[10] Taiwan 22.7%,[16] China 6%[12] and Australia 10%.[18] Again, this may

be attributed to the racial differences among patients. Difference in the methods of performing the test is an additional factor that may have contributed to the difference of rates of positive Pathergy test in various reports.

Ocular involvement is a serious event that may complicate the course of BD. All parts of the eye may be involved, and the spectrum of eye lesions includes uveitis, cataract formation, glaucoma, retinal hemorrhage and retinal detachment. The prevalence of ocular involvement in one study from Turkey was 28.9%,[14] in two studies from Korea the prevalence was 39.5% and 28.5% in Singapore.[9,11] The National Skin Center reported ocular involvement only in 5.9% of patients. In our study we found a higher incidence of ocular involvement (60.8%) which may be a result of genetic and geographic variation. However, high prevalence of eye involvement has been reported in Iran and Taiwan: 61% and 55% respectively.[9,17] In another study from Jordan the prevalence of ophthalmic involvement in BD was reported to be as high as 50%[17] (Table III).

As ocular lesions tend to persist and progress with successive attacks, early diagnosis and prompt treatment may prevent a significant morbidity in these patients. Our high rate may be attributed to increased referral to ophthalmic clinic where all patients had been examined carefully for the presence of any eye lesions. Also the high prevalence of ocular involvement could be due to ocular diseases that were included as BD eye manifestation other than the ones agreed on the criteria.

Inflammatory joint disease in BD may affect the patient's physical ability and impact his quality of life. We found that 43.4% of our patients had joint involvement in the form of arthralgia, arthritis and sacroilitis. The prevalence rates of articular manifestations in BD reported in different studies varies greatly (Table III). This variation is more likely to be a result of a statistical bias of small number of patients in most reports. Another important factor that may also have contributed to these variations is the difference in patient selection. Depending on where and how patients are selected, symptoms and their frequency may vary.

Conclusion

The pattern of cutaneous, ophthalmic and articular manifestation in our group of patients was different from patterns reported in countries with different races and more similar to patterns in neighboring countries. The results may be due to the effect of difference of both the genetic background and environmental factors among different countries.

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