Systemic and Mucocutaneous Manifestations of Behcet's Disease: An Analysis of 107 Cases

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ABSTRACT

Objectives: To study the types and frequency of mucocutaneous and systemic manifestations of Behcet's disease among Jordanian patients.

Methods: A retrospective analysis of 107 patients diagnosed clinically to have Behcet's disease between January 2004 and December 2007 at King Hussein Medical Center was conducted. All Patients fulfilled the International Study Group Criteria for the diagnosis of Behcet's disease. Simple statistical analysis was used.

Results: Eighty-two patients were males and 25 were females, the age range was between 16 and 65 year, 52 (48%) patients' age ranged between 20-29 year, 104 (97%) patients had oral ulceration, 93 (87%) patients had genital ulcers, 99 (92%) patients had skin manifestation were acneiform eruption was the most common finding of skin manifestation, eye involvement was recorded in 34 (32%) patients (17 patients had bilateral uveitis, five had unilateral uveitis, 13 had retinal vasculitis and five were blind, two of whom had unilateral blindness). Arthritis was seen in 64 patients, vascular lesions in 39 patients, and neurological manifestations were seen in 22 patients. Pathergy test was positive in 36 patients. HLA-B51 was positive in 48 patients and negative in 26 patients, while undetermined in 33 patients.

Conclusion: Mucocutaneous manifestations of the disease are common in Jordanian patients. They are similar to other countries in the region in many aspects of diverse manifestations, age of onset and chronicity. Male predominance was noted in this series of cases. Superficial thrombophlebitis was common and morbidity was higher. Intracranial hypertension was more prevalent in patients with neurological manifestations.

Key words: Behcet's disease, cutaneous and systemic manifestations, epidemiology

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Introduction

Behcet's disease (BD) was named in 1937 after the Turkish dermatologist Hulusi Behcet, who first described the triple-symptom complex of recurrent oral aphthous ulcers, genital ulcers, and uveitis. Behcet's disease is a multisystem disease with unpredictable course and almost all organs of the body can be affected concomitantly or consecutively.[1] Behcet's disease is a multisystem polysymptomatic disease including involvement of the mucocutaneous, ocular, cardiovascular, renal, gastrointestinal, pulmonary, urologic, central nervous system, joints, and blood vessels. Behcet's disease is most prevalent in the Mediterranean region (Middle East). The type and frequency of cutaneous manifestation of Behcet's disease is variable and diverse with unpredictable exacerbation and remission.

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The cause of Behcet's disease is not known. However, immunogenetics, immune regulation, vascular abnormalities, or bacterial and viral infection may have a role in its development. There is genetic background with a high prevalence of the disease among people of the Mediterranean, the Middle East, China and Japan. There are occasional familial cases and association with HLA types particularly with HLA-B5 (Bw51 split).[2]

The typical course of Behcet's disease is one of periodic remissions and exacerbations. Over time, the disease typically becomes less severe; but few serious consequences may develop. Current therapies are often somewhat effective, yet frequently complicated by undesirable side effects.

Methods

A retrospective simple statistical analysis of 107 patients diagnosed clinically at King Hussein Medical Center to have Behcet's disease between January 2004 and December 2007 was conducted to define the cutaneous manifestation and other systemic involvement. Patients fulfilled the International Study Group (ISG) criteria for the diagnosis of Behcet's disease (Table I), and analysis of skin lesions was performed by dermatologist.

Results

The 107 patients who were diagnosed with Behcet's disease fit the International Study Group (ISG) criteria, 82 of those were males and 25 were females. Their age ranged between 16 and 65 years. Fifty-two (48%) of the patients' age ranged between 20-29 years and one patient was above 50 years old (Table II). One hundred and four (97%) patients had oral ulcers, 93 (87%) had genital ulcers, and 99 (92%) had skin involvement. Acneiform eruption was the most common finding (Table III). Eye involvement was seen in 34 (32%) patients, 17 of whom had bilateral uveitis, five had unilateral uveitis, 13 retinal vasculitis and three were blind in both eyes and two were blind in one eye. Arthritis was seen in 64 patients.

Vascular lesions were found in 39 patients, 10 of whom had gastrointestinal symptoms of gastritis and esophageal varices. Thrombophlebitis was found in 12 patients, nine had deep vein thrombosis, pulmonary symptoms due to aneurysm or emboli occurred in eight patients. Thrombosis in either superior or inferior vena cava was seen in eight patients. Neurological manifestations were seen in 22 patients, the most common symptom being headache (10 patients) due to increased intracranial pressure. Two patients had meningoencephalitis, three patients had cerebral infarction, three had seizures, and two had peripheral neuropathy. Pathergy test was positive in 36 patients out of 83 (43%) patient tested and 33% of all cases. HLA-B51 allele was positive in 48 patients, negative in 26 patients and undetermined in 33 patients.

Discussion

The cause of Behcet's disease is unknown and there is no specific test to diagnose the disease. As a result, the clinical criteria of ISG are used for diagnosis. These criteria identify the most common features of Behcet's disease throughout the world. Aphthous stomatitis is one of the major criteria and the first symptom of Behcet's disease. Differences in disease manifestations in various geographical regions affect the disease severity.[3] Behçet's disease is endemic among populations clustered along the historic Silk Road, which extended from Eastern Asia to the Mediterranean basin.[4] and Turkey has the highest prevalence of the disease. Behcet's disease is common between the second and fourth decades of life, but can be develop at any age with more severe picture of disease in males and younger age of onset.[5] Prepubertal onset is rare, as is elderly onset (>50 years).[6]

Our patients' age range is consistent with these findings where 89 (83%) patients were between 20-40 years. The male to female ratio was 3.28:1 which is similar to many previous studies.[6,7,8] However, new studies reveal roughly equal incidence in both sexes, with male predominance still persisting in Arab countries,[9] while in an American study the female to male ratios was 1.9:1.[3]

Cutaneous lesions were common and recurrent and these include: erythema nodosum like lesions, acneiform eruptions and thrombophlebitis.[10] The acneiform eruptions and papulopustular lesions usually run normal course and are cleared smoothly. The erythema nodosum was seen in 26 patients and had similar course as non Behcet's associated erythema nodosum. Interestingly Forty-seven patients (47%) had more than one type of skin lesion which is higher than that seen in similar studies where the percentage of patients who had more than one lesion was 21%.[11] Five of our patients had superficial or deep thrombophlebitis; one of them had severe superficial thrombophlebitis with widespread post inflammatory hyperpigmentation.

Table I. The ISG criteria for Behcet's disease [17]

Major criteria (need 1)	Recurrent oral ulceration	Minor aphthous, major aphthous, or herpetiformis ulceration observed by physician or patient that recurred at least three times over a 12-month period
Minor criteria (need 2)	Recurrent genital ulceration	Aphthous ulceration/scarring observed by physician or patient
	Eye lesions	Anterior or posterior uveitis or cells in vitreous on slit lamp examination; or retinal vasculitis observed by ophthalmologist
	Skin lesions	Erythema nodosum observed by physician or patient, pseudofolliculitis or papulopustular lesions; or acneiform nodules observed by the physician in a post adolescent patient who is not receiving corticosteroid treatment
	Positive Pathergy test	As interpreted by physician at 24 to 48 hours

Table II. Age distributions of patients

Age range	No of patients	% of patients
10-19	12	11
20-29	52	48
30-39	37	35
40-49	5	5
50-59	0	0
60-69	1	1

Table III. Cutaneous manifestations of Behcet's disease

Skin manifestations	No of patients	% of patients
Acneiform eruption	53	50
Erythema nodosum	26	25
Psuedofolliculitis	13	12
Papulo pustulosis	12	12

Table IV. The different manifestations of Behcet's disease

Clinical feature	Number of patients	%
Oral ulceration	104	97
Genital ulceration	93	88
Skin manifestations	99	92
Eye involvement	34	32
Arthritis	64	60
Neurological manifestations	22	20
Vascular lesions	39	36
Pathergy	36	33

One patient developed unilateral eye blindness four years after onset of Behcet's disease followed by blindness of other eye after 20 years. Twenty two patients had neurological manifestations, ten of them had headache at presentation due increased intracranial pressure, three developed meningoencephalitis presenting with headache and fever, three patients developed cerebral infarcts, three had seizures and two presented with peripheral neuropathy.

A higher rate of positivity of Pathergy test (84-98%) was found more frequently in Mediterranean areas, compared to the Far East (40-70%), or Western countries. Our results were positive for 36 out of 107 cases (33%) and 43% of the 83 tested patients which is comparable to studies around our region. A positive Pathergy test is characterized by the formation of a pustule greater than 2mm at the site of injury within 24 hours.[12,13]

The earliest mucocutaneous lesions were the oral ulcers which ranged from multiple small painful to less frequent herpetiform ulcers. They preceded other systemic involvement by an average of 4.8 years which was less than that seen in other comparative studies.[14,15] but this is comparable with the study done in our region by Al-aboosi and colleagues.[16] Patients usually presented with oral aphthae (minor >major > herpetiform), which may be the only manifestation of disease for six to seven years before any major manifestation is apparent. Gastrointestinal involvement affects 3-16% of patients with Behcet's disease. Areas affected often include the esophagus and ileocecal area with symptoms included abdominal pain, bloating, and

GI bleeding. Complications often result from deep ulceration of intestinal sections.

Arthritis in most of our patients was non erosive symmetrical arthropathy with most of the symptoms at the time of acute attacks of mouth ulceration. HLA-B51 is significantly associated with Behcet's disease in Japan, Korea, Turkey, and France. Our results were similar to those in neighboring countries and higher than an American study.[3]

Many systemic diseases with mucocutaneous manifestations may have similar presentation like Behcet's disease including bollous diseases, connective tissue diseases, erythema nodosum and sweet syndrome; the differentiation made based on the clinical criteria of international study group.

Many patients with Behcet's disease go into complete remission with the passage of time. No standard therapy for Behcet's disease is present. Treatment options according to severity of symptoms where: topical measures for cutaneous manifestations and systemic corticosteroids and immunosuppressant medications for severe systemic involvements.

Conclusions

Mucocutaneous manifestations of Behcet's disease in our study sample were similar in many aspects to studies from around the world, but differ in persistence of male preponderance, prolonged morbidity of cutaneous manifestations, and higher percentage of increased intracranial pressure in patients who presented with headache.

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