Clinical spectrum of Behcet's disease among patients seen at the tertiary rheumatology clinic

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Abstract

Background: Behcet's Disease (BD) is a variable vessel vasculitis with heterogeneous clinical features. Although BD occurs worldwide, it is more common in populations along the Old Silk Road, stretching between the Mediterranean basin, the Middle East and Far East. The prevalence of BD is usually higher in populations with the highest frequency of HLA-B51. Although classical manifestations are mucocutaneous lesions, arthritis and uveitis, it can also affect vessels, nervous system and the gastrointestinal tract.

Objectives: The aim of the research was to study the presentations of Behcet's Disease (BD) in the Saudi population and to determine any differences in clinical manifestations between men and women.

Methods: This was a prospective study involving 16 BD patients seen at the outpatient rheumatology clinic of King Abdul-Azeez Specialist Hospital, Sakaka, Saudi Arabia. They were reviewed to analyze the frequency of different disease manifestations.

Results: Sixteen patients with diagnosis of BD were identified among 840 patients seen in the out-patient clinic. They were mainly Saudi indigenes. All the 16 Saudi indigenes with Behcet's disease satisfied the International Study Group (ISG) criteria and allowed us to obtain a prevalence rate of 1.9%. Twelve men and four women were diagnosed as Behcet's patients, with a mean age of 29 ± 3 years. The median duration of disease at presentation was 4 years (range 1–7 years). Mucocutaneous manifestations were present in all the 16 (100%) patients, ocular manifestations in 7 (43.75%) patients, vascular manifestations in 5 (31.25%) patients, and neurological manifestations in 3 (18.75%) patients.

Conclusion: Behcet's disease among the Saudi population was found not to be an aggressive disease. Ocular complications are mild and responded well to treatment.

Key words: Behcet's disease, Vasculitis, Saudi indigens, Clinical manifestations, Pathergy test, Azathioprine

Introduction

Hulusi Behcet, a dermatologist first described the disease in 1937, as the triad of recurrent oral aphthous ulcers, genital ulcers, and uveitis[1]. It is a chronic multisystem disorder, the cause of which is unknown. The disease can affect nearly every system and organ including ocular, cardiovascular, gastrointestinal, renal, pulmonary, urologic, central nervous systems and joints[2].

Recurrent oral ulcers are the most common clinical manifestation of Behcet's Disease (BD) and usually present in almost all patients[2]. Although BD occurs worldwide, it is however most common in the Mediterranean basin, the Middle East, and the Far East. The prevalence of BD is usually higher in populations with the highest frequency of HLA-B51[3]. Those aged 20 to 40 years are commonly affected. While an equal male-to-female ratio is more common males predominate in Iraq, Jordan, Saudi Arabia, and Lebanon, and females in the USA and Britain[4].

The diagnosis of the BD relies on clinical criteria because there are no specific diagnostic laboratory tests or histopathologic findings. The initial clinical manifestations are variable with some patients presenting with mucocutaneous while others systemic involvement. The overall combinations of clinical features are very heterogeneous and can varyfrom patient to patient[5]. Hence a definitive diagnosis may be delayed for several years.

Various diagnostic criteria and classifications have been proposed in the past years. The International Study Group criteria of 1990 stipulate the presence of oral aphthous ulcerations and two of the following clinical manifestations for the diagnosis of BD: recurrent genital ulcerations, skin lesions such as erythema nodosum-like lesions, papulopustular lesions, ocular involvement, and positive pathergy test[6].

Clinical involvement in BD determines the prognosis and the disease may result in considerable morbidity. Loss of visual acuity and neurological disease are major causes of morbidity. Early onset

disease, male sex and HLA B51 positivity are associated with more severe disease[7].

Materials and methods

Study setting: The study was conducted at the King Abdul-Azeez Specialist Hospital, Sakaka, Saudi Arabia, a tertiary hospital catering for the people of Sakaka and environs.

Patients and methods: The study involved patients with Behcet's disease attending the rheumatology outpatient clinic from June 2018 to May 2019. Patients were referred from urban hospitals and from the region of Sakaka. Newly diagnosed and follow-up patients were included and all satisfied the criteria of the International Study Group for Behcet's disease[6].

Detailed histories and clinical presentation were obtained and demographic data including age, sex, occupation, marital status and religion recorded. Particular attention was paid to differences in clinical presentations between males and females. Laboratory investigations performed included complete blood count, Erythrocyte Sedimentation Rate (ESR), liver and kidney function tests. Pathergy test was also carried out. Various radiological investigations to confirm the diagnoses of organ involvement were carried out including doppler, MRI brain. slit lamp and fundus examination.

Results

Sixteen patients (12 men and 4 women) were diagnosed with BD among 840 patients attending our rheumatology clinic between June 2018 and May 2019 a prevalence of 1.9%.The male to female ratio was 3:1 and the mean age at diagnosis was 29 ± 3 years. The median duration of disease at presentation was 4 years (range 1–7 years). Demographic data and laboratory investigations of the patients are shown in Table 1 and the clinical manifestations in Table 2. Most of our patients developed the disease during the third decade of life. Exceptions were one patient aged under 20 and two over 30 years.

Table 1: Demographic data and laboratory investigations of Behcet's patients

	Male	Female
Age (years)	18-34	23-33
Sex	12	4
Smokers	10	0
Age at onset (years)	28 ± 6.5	27 ± 5.5
Disease duration (years)	4 ± 2.2	4 ± 1.5
Haemoglobin (g/dl)	12.2 ± 2.3	11.4 ± 1.1
Platelets ($x10^3$ /mm^3)	256 .3 ± 61.5	261.3 ± 66.5
Total white cell count ($x10^3$/mm^3)	7.5 ± 2.1	7.1 ± 1.9
ESR (mm/hr)	24 ± 11.2	21 ± 12.3
AST (U/L)	23.1 ± 7.3	21.1 ± 6.8
ALT (U/L)	29.4 ± 8.5	28.8 ± 7.4
Urea (mg/dl)	18.2	16.5
Creatinine (mg/dl)	0.85 ± 0.19	0.82 ± 0.15

Table 2: Clinical characteristics of patients with Behcet's disease

Clinical feature	No.	(%)
Systemic symptoms		
Fever	4	25
Fatigue	3	18.8
Oral ulcers	16	100
Genital ulcers	13	81.2
Skin lesions		
Papulopustular	6	37.5
Follicular	1	6.25
Erythema nodosum	2	12.5
Positive pathergy test	7	43.8
Ocular lesions		
Anterior uveitis	3	18.8
Posterior uveitis	2	12.5

Clinical feature	No.	(%)
Neurological involvement	3	18.8
Vascular		
Deep venous thrombosis	2	12.5
Arterial thrombosis	1	6.25
Intestinal involvement	7	43.8
Arthritis	8	50
HLA-B51 positivity	7	43.8

Fever was the predominant systemic symptom followed by fatigue. The majority of the patients presented with oral ulcers as their first symptom apart from two with genital ulceration. Thirteen patients (81%) ultimately developed genital ulcers. Four males and one female developed ocular disease generally within a few years of disease onset. Following referral to ophthalmology, early improvement was noted.

Other observed clinical manifestations were; arthritis (50%), skin lesions (56%), central nervous system (18.8%), pulmonary manifestation (25%), deep venous thrombosis (12.5%), gastrointestinal manifestations (43.8%), and epididymitis (0.06%). The pathergy test was positive in 7 of 16 (43.8%) patients and HLA B51 was positive in 9 of 16 (56%) patients.

There was no significant difference in the clinical manifestations between men and women aside from the ocular manifestations. All the patients were placed on azathioprine. Some patients received corticosteroids both oral and topical when indicated.

Discussion

In this study, disease patterns and morbidity of BD patients were analyzed. The period prevalence of BD disease among our rheumatic disease patients at the time of the study was 1.9%. The male to female ratio among the study population was 3.1. Gender distribution in BD patients differs widely depending on their ethnic origin and country of residence[8]. The frequency of male patients diversely ranged from 27% in USA to 87% in Azerbaijan. Studies have found a higher frequency of male patients in North African and sub Saharan African in comparison to those from Europe[9].

The prevalence of BD among females in our study may not reflect the true picture because of religious practice and a reluctance of females to seek medical advice for genital ulcers, especially when faced with a male or a foreign practitioner. There is therefore the potential for under-diagnosis of BD in Saudi females.

In our study, mucocutaneous manifestations were the leading manifestations. All patients reported oral ulcers and 13 developed genital ulcers and[9] skin lesions with papulopustular lesions predominating. In general, the mucocutaneous lesions are in agreement with other studies with the overall frequency of oral ulcers ranging between 95% and 100% of the BD patients[10].

An oral lesion was the first presentation in 11 patients and genital lesions in 5 patients. Studies have documented oral lesion as the first manifestation in about 25 -75% of cases[11]. Studies from Egypt reported oral lesion as the first presentation in 80% and 84.2% respectively[12,15]. Genital ulcers were present in 81.25% of patients. Genital ulcers are reported to be the second most common manifestation present in a large percentage of BD patients and have been reported in different frequencies from 62% to 100% of patients[13]. Egyptian studies recorded a range of 76% to 96.8%[14,15].

Ocular involvement occurred in 5 (31.25%) of patients a prevalence at the lower end of the 30-70% frequencies reported by Alpsoy *et al*[16]. Uveitis was the predominant ocular lesion and usually noticed in the first four years from onset of the clinical manifestations. The ocular lesions responded well to treatment without any permanent visual loss. In one of these five patients the ocular lesion was the presenting manifestation in agreement with the studies of Ayman e*t al*[17] and Al Dalaan *et al*[18]. Onset of ocular manifestations is usually noticed 2-4 years of onset of Behcet's disease. Uveitis is the commonest form of ocular involvement; the anterior segment is usually affected first and initially unilateral. Posterior segment and bilateral involvement usually occurs later[16].

Thrombosis was the main vascular lesion constituting 18.75% of our cases. Vascular lesions were recorded at 5.4% in Singapore[19] and range from 9% to 37% Japan and Turkey[20]. Vasculitis in BD may involve the small, medium and large vessels and can affect both the arterial and venous sides of the circulation[19]. Venous lesions are the most frequent and may present with both deep vein or central vein thrombosis. Arterial involvement is mainly in the form of aneurysms and occlusions.

Three patients presented with neurological involvement, representing 18.75% similar to studies from Japan (11%)[21], Germany (11%)[22] and Tunisia (12%)[23]. In Egyptian studies, the frequency is higher (26.3%)[12]. Neurological involvement occurs in 5–30% of BD patients and is the initial presentation of the disease in about 5–23% of patients[24].

Seven (43.75%) of our patients presented with gastrointestinal complaints. The abdominal presentations included abdominal pain, dyspepsia, diarrhea, vomiting and small bowel ulcers. The frequency of gastrointestinal system involvement is variable in different countries[25].

Gastrointestinal manifestations occur in one-third of Japanese patients, while in Turkey and Israel, the prevalence is about 0–5%[26].

Articular involvement is observed in the form of arthralgia or arthritis. In our study five patients developed arthritis mainly mono articular and three arthralgia. Both lower and upper joints were affected but the toes and the fingers were spared. Articular involvement is seen in approximately 30–70% of BD and may be the first manifestation of the disease in about 16.5% of them[27]. The knees, ankles, wrists, and elbows are commonly affected. When oligoarticular involvement is seen, it is usually asymmetrical. Arthritis is usually transient, nonerosive, and nondeforming. Chronic or polyarticular arthritis can be seen occasionally[28].

In conclusion this was a relatively small hospital based study of Saudi patients with BD, all the classical clinical features of BD were encountered. Overall, the general prognosis including ocular disease was good possibly because of early presentation to secondary care and availability of free medications. There were no significant differences seen in the clinical presentations between the male and female genders except in ocular presentation.

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Conflict of interest: The authors declare that there is no conflict of interest as regards to this study.

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