BehÇet's disease in Libya

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Abstract

Introduction: Behcet's Disease (BD) is a chronic, relapsing, inflammatory disease characterized by recurrent oral aphthous ulcers and numerous potential systemic manifestations. In Libya, no previous studies were done on BD.
Objective: To study the different clinical manifestations of BD in Libyan patients and compare them with other countries and to compare the behaviour of BD among female and male patients.
Methods: The study was done retrospectively on a cohort of 100 patients with a diagnosis of BD who were registered in our rheumatology clinic in Tripoli Medical Center during the period between 1999 and 2009. The data which were collected from the files of patients included demographic features (such as sex, age at diagnosis and disease duration), different clinical manifestations of the disease which occurred either initially or as a late feature and types of relapses.
Results: One hundred patients enrolled in the study, 71% were male and 29% were female, the ratio of female to male was 1: 2.4. The mean age was 31 years. The prevalence of various clinical manifestations were oral ulcers: 100%; genital ulcers: 81%; skin: 42%; ocular: 35%; vascular: 31%; arthritis: 23%; CNS: 32% and positive pathergy test: 21%. The most common initial manifestations of BD on presentation were oral ulcers: 99% and genital ulcers: 80%. The most common late features which occurred after months to years after diagnosis were recorded in 38 patients (38%), were; CNS: 58%, vascular: 31% and ocular: 21%. Relapses occurred in 62% of patients, the most common types were oral ulcers: 60% and CNS relapses: 35%. Eye involvement occurred in 35% and 34% in male and female respectively (p-value=0.89). CNS involvement occurred in 32% and 31% in male and female respectively (p-value = 0.94). Relapse rate was 59% in male and 69% in female (p-value=0.35).
Conclusions: CNS manifestations are more common among our patients which is similar to other Arab countries (Egypt and Jordan) but significantly more than other countries like Turkey, some European countries (Italy and Germany) and USA. Male and female have similar prevalence of clinical manifestations (CNS, eye and vascular) and similar relapse rates.

Key word: Behcet's Disease (BD), Central nervous system involvement (CNS), Relapse

Introduction

Behcet's Disease (BD) is a chronic, relapsing, inflammatory disease characterized by recurrent oral aphthous ulcers and numerous systemic manifestations, including genital ulcers, ocular disease, skin lesions, neurologic disease, vascular disease and arthritis. BD may have been described by Hippocrates, but was brought to the attention of the modern medical community by Hulusi Behcet's in 1937[1-3].

The disease occurs endemically in the eastern Mediterranean and in the middle and far eastern countries, the population deriving from the ancient Silk Road. The highest prevalence was reported in Turkey, with familial occurrences reported from endemic area[4]. BD has a higher prevalence in men than in women. Usually the onset occurs in the third decade of life.

It is rarely seen in children and has more aggressive course in young adults (male)[5]. The diagnosis of BD is based on clinical criteria as established by an International Study Group. These criteria omit the less certain and less common features of the disease[6]. Both innate and adaptive immune systems are activated in BD, with a pro-inflammatory and Th1-type of cytokine profile. BD may be linked to a specific primary immune abnormality with a genetic mutation affecting an adhesion molecule or a pro-inflammatory cytokine, which predispose to early or more intense neutrophil and T cell responses[7]. The greatest morbidity and mortality occur with ocular disease (affecting up to two thirds of patients), vascular disease (affecting up to one third of patients) and central nervous system disease (affecting 10-20% of patients). Cutaneous and articular manifestations are common. Renal and peripheral nervous system involvement are less common than in other vasculitides[8]. BD has a highly variable clinical course with recurrences and remissions. In the absence of neurological, ocular and vascular

involvement, the disease is generally benign and with a good prognosis. Blindness, which occurs in up to 25% of the patients, is the major cause of permanent disability[9]. In Libya, the total number of patients with connective tissue disease who were registered in our rheumatology clinic in Tripoli Medical Center from 1999-2009 were 2000 patients. One hundred of them had BD. No previous studies were done in Libya on BD. The primary reason of this study was to know the frequencies of clinical manifestations of the disease in our patients and compare them with other countries and secondly to compare the behaviour of BD among female and male.

Materials and Methods

This study was done retrospectively on a cohort of 100 registered patients with the diagnosis of Behcet's disease who were registered in our rheumatology clinic in Tripoli Medical Center during the period between 1999 and 2009. All patients were seen by a rheumatologist, ophthalmologist and a dermatologist. Patients were seen by a neurologist when necessary. Diagnosis was based on the clinical picture of the disease and the clinical judgment of at least two rheumatologists and not only on particular diagnostic criteria. The majority of the cases however, were classified by international study group diagnostic criteria. The data which were collected from the files of BD patients includes demographic features (such as sex, age at diagnosis and disease duration), clinical manifestations which occurred at any time of the disease, clinical features which occurred at presentation (initial features) or developed after months to years after diagnosis (late features) and types of relapses (either a relapse of initial features or occurrence of new features). Relapse rates among male and female patients were recorded.

The results were analysed statistically using the Statistical Package for Social Sciences version 11 computer package (SPSS Inc., Chicago, IL., USA). Comparison between clinical features in male and female was done and p-value < 0.05 was considered significant. Comparison between clinical features (eye-CNS-vascular) of our patients with other countries using a graph illustrating a proportion of our patients at the 0 line and percentage of patients using 95% confidence intervals. If the percentage of patients of other countries above 0 line that means specific clinical feature in patients of that country more than our patients. If it crosses the 0 line, it means the percentage of clinical feature of patients of that country similar to our patients. If it is below 0 line, it means that the percentage of patients of that country is less than our patients.

Results

The total number of patients registered in our rheumatology clinic in Tripoli Medical Center were 2000. One thousand two hundred (60%) patients had rheumatoid arthritis, 400 (20%) had systemic lupus erythematosus, 200 (10%) patients had systemic sclerosis, 60 (3%) patients had ankylosing spondylitis, 40 (2%) patients had mixed connective tissue disease and 100 (5%) patients had BD.

The mean age of patients with BD was 31 years. The male to female ratio was 2.4:1 and the mean disease duration (duration from date of diagnosis until last review) was 6.6 years. Clinical manifestations of BD which occurred either initially (which present at diagnosis or as late features (which occurred months to years after diagnosis) were distributed as following, oral ulcers in 100%, genital ulcers in 81%, skin involvement in 42% (as acne like lesions 67%, erythema nodosum 28% and folliculitis 26%), eye manifestations in 35% (as posterior uveitis 54%, anterior uveitis 46% and retinal vasculitis 23%), CNS features in 32% (as headache 34%, hemiparesis 31%, cranial nerve palsy 22% and cerebellar ataxia 16%) vascular involvement in 31%, arthritis in 23%, pathergy test was positive in 21% and there was no GIT manifestations occurrence in our patients (Table 1).

Table 1: Distribution of BD clinical manifestations in the world

Country	No.	OA	GA	Skin	Eye	Joint	CNS	GI	Vas
Libya	100	100	81	42	35	23	32	-	31
Iran	5059	97	65	69	56	34	3.2	8	8.5
Saudi Arabia	119	100	87	57	65	37	44	4	25
Iraq	100	100	91	74	39	49	13	7	21
Jordan	200	99.5	86.5	90.5	42	47	38.5	17	-
Israel	91	100	77	79	52	78	14	15	26
Egypt	274	92	76	39	76	50	26	10	-
Morocco	673	100	84	-	67	57	14	-	19
Turkey	2147	100	88	-	29	16	2.2	2.8	11
Italy	155	98	73	86	92	77	17	34	18
Germany	415	98	65	74	51	53	-	-	-
England	419	100	89	86	68	93	31	7	22
USA	164	98	80	66	70	42	21	8	19

No.: number of cases; OA: % of oral aphthosis; GA:% of genital aphthosis; Eye: % of ocular lesions; CNS: % of central nervous system involvement; GI:% of gastrointestinal manifestations; Vas:% of vascular involvement.

The most common initial manifestations were oral ulcers (99%). Other initial features occurred as following; genital ulcers in 80%, skin lesions in 45%, eye involvements in 27%, arthritis in 24%, vascular manifestations in 16% and the least common initial manifestations were CNS features 9%. The most common late features which occurred from months to years after diagnosis in 38 (38%) patients, were CNS involvement (22/38) 58%. Other late features were vascular manifestations in 31.5%, eye lesions in 21%, skin lesions in 7%, genital ulcers in 7%. The least common late features were oral ulcers (1/38) 2.6% and no patient developed arthritis as late feature. Sixty two per cent of our patients had relapses (either relapse of initial features or development of new manifestations as late features) and 38% had no relapses. Types of relapses occurred as following; relapse of oral ulcers occurred in 60% of patients, relapse of CNS features occurred in 35.4%, relapse of genital ulcers occurred in 29%. Relapses of skin lesions, eye lesions, vascular involvements and arthritis occurred in 26%, 22.5%, 22.5% and 6% respectively. Clinical features in both male and female were studied and no significant differences were found. They were similar in oral ulcers (100% in both), genital ulcers (86%, 68% respectively), skin features (41%, 44% respectively) and arthritis (21%, 27% respectively) p-value>0.05. Even serious clinical manifestations of BD (CNS, eye and vascular) were similar in male and female. CNS features occurred in 32% of male and 31% of female (P-value=0.9). Eye involvements recorded in 35% of male and 34% of female (p-value=0.9). Vascular manifestations occurred in 37% of male and 17% of female (p-value=0.06). Relapse rate in male was 59% and relapse rate in female was 69% which were also similar (p-value=0.35).

Discussion

Behcet's Disease (BD) has different clinical manifestations in different countries. This difference might be related to different distribution of susceptibility gene for the disease (HLA B51) in the world. There are many reports on clinical manifestations of BD from different parts of the world[10-24]. Comparison between clinical features of BD patients in our country and other countries were shown on Table 1.

Regarding CNS manifestations (Figure 1), our patients have a higher frequency of CNS involvement (32%) similar to BD patients in Jordan, Egypt, Saudi Arabia, Iran and England.

Vascular manifestations (Figure 2), in our patients had a frequency similar to Saudi Arabia, Iraq and England patients. Iran has more vascular involvement among their patients. Eye manifestations (Figure 3) in our patients are less than other countries (Iran, Saudi Arabia, Egypt, Morocco, Italy, Germany and England) but similar to Iraq, Jordan, Turkey and USA. Our data show more similarity with those of Jordan, Saudi Arabia and Iraq than with the western parts of the world. Oral aphthae or canker sores are often the initial features of Behcet's disease[25].

Figure 1: Comparison of CNS involvement between Libya and other countries

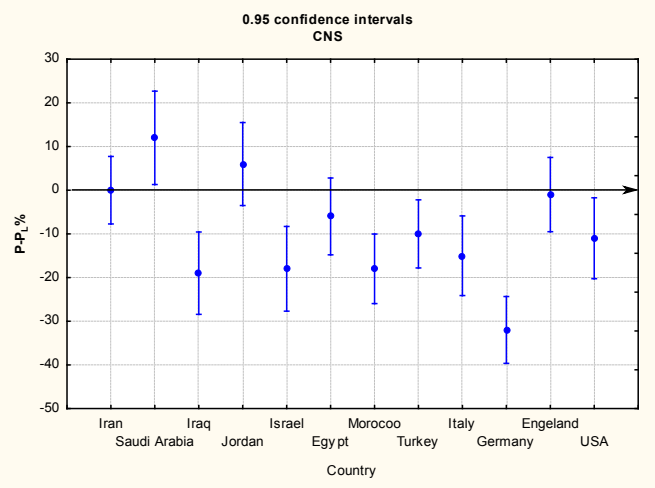


Figure 2: Comparison of vascular involvement between Libya and other countries

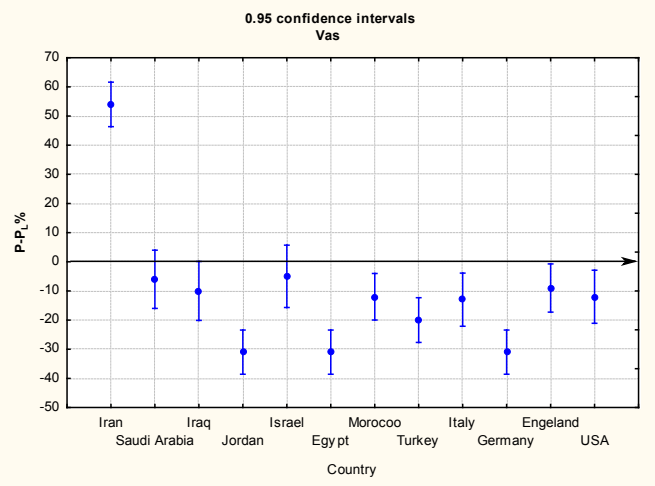
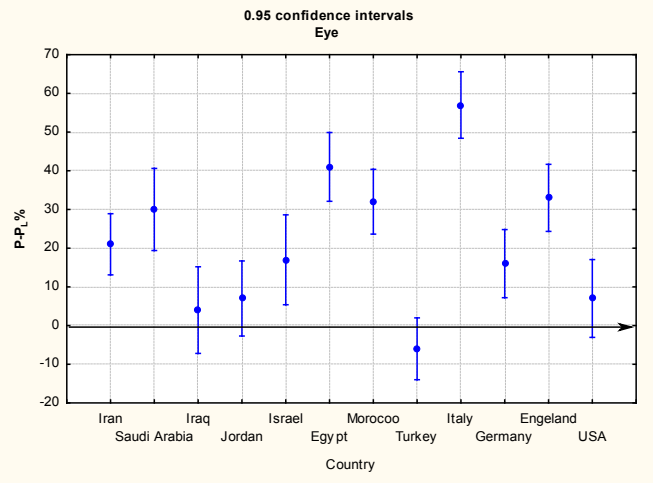


Figure 3: Comparison of eye involvement between Libya and other countries



Ninety nine per cent occurred on our patients. Other features like neurologic involvement, they often appear late in the progression of the disease but are associated with poor prognosis. Collectively, neurologic symptoms tend to be an unusual late manifestation, 1-8 years after the disease onset[26]. In Behcet's disease, presentation in males serves as the only proven predictor of severity,

causing many of the complications of BD in higher proportion to their female counterparts[27]. But with our patients, we noticed a similar clinical presentations and similar relapse rates in both female and male. Vascular complications develop in about 20-40% of patients with BD [28,29]. Pulmonary involvement is relatively infrequent, having been reported in 1%-10% of patients[28,30,31]. Vascular involvement occurred in 31/100 (31%) of our patients and 2/31 (6.4%) had pulmonary artery aneurysm. They were males and one of them died because of severe pulmonary haemorrhage and the other one is still alive after a left pneumonectomy operation. BD is the most common cause of pulmonary artery aneurysm[32]. Aneurysm formation in the pulmonary arteries indicates a poor prognosis: 30% of patients with this condition will die within 2 years[30,33,34].

Conclusion

CNS manifestations are more common among our patients which is similar to other Arab countries (Egypt and Jordan) but significantly more than other countries as Turkey, some European countries (Italy and Germany) and USA.

Both male and female have similar prevalence of clinical manifestations (CNS, eye and vascular) and similar relapse rates.

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