Comparison of Clinical Features of Behcet Disease According to Age in a Tunisian Cohort

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Received: 23 May 2013; Accepted: 5 Jan. 2014

Abstract- Behcet's disease (BD) is a multisystemic inflammatory disease that occurs most often between the second and fourth decade of life. Patients have been reported during the first months of life and after 70 years. Our objective was to determine the clinical, paraclinical and genetic characteristics of BD in patients aged < 20 and > 40 years. We conducted a comparative retrospective study including patients with BD (Criteria of International Study Group on BD). Patients were divided into two groups: those < 20 years (Group one) and those > 40 years (Group two). The clinical, paraclinical and genetic (HLA) characteristics were determined and compared in the two groups. The data were compiled and analyzed using SPSS 11.0. Thirty totals of 430 patients were included. Group one included 81 patients (55 men and 26 women). Group two included 68 patients (45 men and 23 women). Cutaneous involvement (88.9 versus 76.5%; *P*=0.043), pseudofolliculitis (84 versus 64.5%; *P*=0.004) and vena cava thrombosis (11.11 vs 0%; *P*=0.004) were significantly more frequent in group one while joint involvements were more common in group two (57.4 versus 40.7%; *P*= 0.043). The frequency of erythema nodosum as well as ocular, vascular and neurological disorders was comparable between the two groups. Few studies in the literature have compared the clinical, paraclinical and genetic characteristics of BD, who had first symptom onset after 40 years of age. Late-onset BD, usually, affects both genders equally. According to present results, the frequency of severe organ involvement is equal regardless of age, except for vena cava thrombosis.

Acta Medica Iranica, 2014;52(10):748-751.

Keywords: Behcet disease; Age; Late onset; Clinical features

Introduction

Behçet's Disease (BD) is a multisystemic inflammatory disorder characterized by oral and genital ulcers and cutaneous, ocular, arthritis, vascular, central nervous system and gastrointestinal involvement. The disease is most common along the ancient Silk Road extending from Eastern Asia to the Mediterranean basin. The typical age of onset is the 30s, and the male to female ratio varies with ethnic origin (1,2). Diagnosis of the disease relies solely on the identification of clinical features as defined by criteria outlined by the International Study Group for BD (3). Its main morbidity is related to blindness due to repeated attacks of ocular inflammation, whereas involvement of the central nervous system or major vessels may be serious enough to lead to death (4).

The young adult is the most affected, with a typical onset between the age of 20 and 40 years (5), varying from the first few months of life to the age of 70 years (6), but BD is still exceptional after the age of 60 years.

Late onset BD still is not well defined (7); it, usually, affects both genders equally. The frequencies of severe organ involvement are higher before 20 years. Given the scarcity of patients after 60 years, the purpose of this study was to compare clinical, and severity properties of BD between patients aged <20 years and those >40 years.

Materials and Methods

We performed a comparative retrospective study including patients with BD recruited from the Department of Internal Medicine, Hospital la Rabta in Tunis, over a 20-years period (1989-2009). Diagnosis of BD was made according to the criteria of the International Study Group for BD (ISG).

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They were 295 men and 135 women with a mean age of 29.12±10.241 years. All clinical manifestations were recorded on a standard form. The clinical features of the patients are summarized in Table 1.

Table 1.Characteristics of the 430 patients

Clinical features	Patients (n = 430) N (%)
Oral ulcers	430 (100)
Genital ulcers	341 (85)
Pseudofolliculitis	320 (74.4)
Positive pathergy test*	176/305 (57.7)
Arthritis/Arthralgia	195 (45.7)
Ocular involvement	200 (46.5)
Neurological involvement	140 (32.6)
Vascular involvement	150 (34.9)
Deep vein thrombosis	136 (31.6)
Arterial aneurysms	23 (5.3)
Arterial thrombosis	6 (1.4)
Intestinal involvement	7 (1.6)
HLA B51 +	84/177 (47.5)

Patients were furthermore divided into two groups: those younger than 20 years (group one) and those aged over 40 years (group two). The clinical, paraclinical and genetic characteristics (HLA) were compared between the two groups. The mean duration of followup was 10.5 years (3-23 years).

The onset of BD was defined as the time when the first symptoms attributed to the disease occurred.

Statistical analysis

Data were recorded and analyzed using SPSS 11.0. Statistical analysis was made by independent samples *t*-test and chi-square test.

Results

Group one included 81 patients (55 men; mean age 17 years). Group two included 68 patients (45 men; mean age 47 years). There was no significant difference regarding the gender between the two groups. The mean age of onset BD disease was significantly lower in group, 1:16.12± 3.709 years vs. 45.49 ± 4.955 years; *P*= 0.01.

Cutaneous involvement (88.9 vs 76.5%; *P*=0.043), pseudofolliculitis (84 vs 63.2%; *P*=0.004) and vena cava thrombosis (11.11 vs 0%; *P*=0.004) were significantly more frequent in group one, while joint involvements were significantly more frequent in group two (57.4 vs 40.7%; *P*= 0.043). The frequency of erythema nodosum, positive pathergy test, ocular, vascular and neurological disorders were comparable between the two groups. No significant difference was between the two groups regarding the HLA B51 positivity. All these results are shown in table 2.

Table 2. Comparaison between the 2 groups

	Age <20 N= 81 (%)	Age > 40 N=68 (%)	*p*
Males /Females	55/26	45/24	NS
Age of disease onset	16.12+/- 3.709	45.49 +/- 4.955	0.01
Genital ulceration	76.5	80.9	NS
Cutaneous involvement	88.9	76.5	0.043
Pseudofolliculitis	84	63,2	0.004
Erythema nodosum	18,5	17.6	NS
Pathergy test	55.7	50	NS
Ocular involvement	44.4	36.8	NS
Uveitis	43.2	32.4	NS
Retinal vasculitis	28.4	29.4	NS
Visual loss	6.1	10.2	NS
Articular involvement	40.7	57.4	0.043
Neurologic involvement	22,2	25	NS
Seizures	3.7	0	NS
Parenchymal involvement	14.8	14.7	NS
Vascular involvement	32.1	36.8	NS
Lower limb	22.22	22.05	NS
Vena cava	11.11	0	0.004
Venous Thrombosis	30.9	30.9	NS
Arterial Aneurysm	2.5	4.4	NS
HLA B51	51.7	53.6	NS
Mortality	2.46	NS	

Discussion

In current study, cutaneous involvement (88.9 versus 76.5%; *P*=0.043), pseudofolliculitis (84 versus 64.5%; *P*=0.004) and vena cava thrombosis (11.11 vs 0%; *P*=0.004) were significantly more frequent in the patient < 20 years, while joint involvements were more common in those > 40 years (57.4 versus 40.7%; *P*= 0.043). The frequencies of erythema nodosum, as well as ocular, vascular and neurological disorders were comparable between the two groups. This is in contrast with the knowledge that BD runs a more severe course among those developing the disease at a young age. However, the more severe course of vascular BD in young is confirmed in the present study. That is consistent with the well known difference in clinical BD presentation according to the studies' population. Perhaps this is why some prefer to call Behçet a syndrome rather than a disease.

BD is common in the second to fourth decades of life, but it can be seen at any age. Prepubertal onset is rare, as the elderly onset (>50 years).

In the review of the literature done by Ziadé *et al*., (7), the mean age of onset of the first symptoms in BD sw between 26 and 34 years of age. The mean age of onset was 25.6 years in Turkey (2147 patients) (4), 28.8 years in Korea (1155 patients) (8), 27.5 years in Tunisia (702 patients) (5) and it was 29 years in present study (430 patients).

When considering the extreme ages of onset, the disease may start in the first few months of life until the age of 54 years in the Mediterranean basin, in Europe and the Arab countries (4- 6,9-12). It may start as late as the age of 72 years according to studies conducted in Asia (8,13). However, onset after the age of 60 years is exceptional.

For Citirik *et al*., late-onset BD showed a marked preponderance of males with a sex ratio of 3:1 (14).

Literature on frequency and severity of symptoms of BD is conflicting, which may be the result of differences in geographic and ethnic origin of the patients, use of different diagnostic and age criteria, and variations in the study design. Since the course of the disease is regarded to be relatively mild in mature patients, it is noteworthy that systemic manifestations such as ocular and neurologic involvement and acute flares developed after the age of 50 years in the limited number of patients with late-onset BD in the series of Saricaoglu *et al*., (15).

Some authors found that the early onset, before the age of 25, seems to be associated with more ophthalmic manifestations and active course of the disease (8,13).

Tsai indicated that the clinical course of BD is not indolent in the patients with late-onset BD. He reported no significant difference in clinical profiles between patients with disease onset before and after 40 years of age, but the incidence of uveitis, an indicator of unfavourable prognosis, was surprisingly high (16).

More importantly, physicians should be aware that BD can occur in older patients, and close attention regarding their disease activities is warranted as their clinical courses may not be as benign as previously believed.

We found that cutaneous involvement were more observed in patients younger than 20 years, to our knowledge this was not reported previously in the literature. On the other hand, articular involvement was more frequent in patients older than 40 years.

When studying 42 patients with BD onset after 40 years of age, Sungur *et al*., concluded that late-onset BD, usually, affects both genders equally, and the prognosis of ocular involvement is, usually, good. The incidence of panuveitis decreases as age increases while the incidence of anterior uveitis increases (17).

Concerning the prognosis of the disease according to the age of onset, Saadoun by studying 870 patients with BD found that there was an increased mortality among patient's ages 15-24 years (RR 2.99) and those ages 25-34 years (RR 2.90) as compared with age-and sex-matched healthy controls. The mortality decreased in patients older than age 35 years (RR 1.23) (18).

However, the exact age of late onset disease remains indeterminate. Largest studies are necessary in order to precise the effect of age on the course of BD.

BD affects the young adult but has to be evoqued even in patients younger than 20 years or older than 40 years, to be treating adequately and prevent complications. In current study, the prognosis of BD was similar in the two groups, unlike other studies where the prognosis was worst in patients with juvenile onset of BD. Only an adequate and early treatment may prevent the ophthalmic and severe systemic complications in these patients.

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