Behçet's Disease in Israel: the Influence of Ethnic Origin on Disease Expression and Severity

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ABSTRACT. ***Objective.*** To evaluate the relationship between ethnic origin and manifestations of Behçet's disease (BD) in Israel.

Methods. We studied 100 Israeli patients with BD, 66 Jews and 34 Arabs. The 3 largest ethnic groups of Jewish patients originated from Iran/Iraq (n = 21), Turkey (n = 12), and North African countries (n = 21). Patients were evaluated with respect to the entire spectrum of disease manifestations, and a systemic severity score for BD was calculated for each patient. Disease expression was compared between Jewish and Arab patients and among Jewish ethnic groups.

Results. There were no statistically significant differences between Jewish and Arab patients with respect to male:female ratio, prevalence of HLA-B5, age of disease onset, or disease duration. Disease expression and severity score were also similar in the 2 groups, but Arab patients had a higher rate of posterior uveitis (20.6 vs 4.6%; $p < 0.03$). Among the 3 largest Jewish ethnic groups, patients of North African origin had a significantly higher rate of ocular disease ($p < 0.01$), mainly in the form of anterior uveitis ($p < 0.01$). These patients also had higher rates of arthritis, overall vascular disease, deep vein thrombosis, and neuro-Behçet without reaching statistical significance. The disease severity score in this group was significantly higher compared to the other Jewish ethnic groups ($p < 0.02$).

Conclusion. The expression of BD is similar in Israeli Jewish and Arab patients but the latter have more severe eye disease. The disease in Israeli Jewish patients is most severe in those originating from North African countries. (J Rheumatol 2001;28:1033–6)

Key Indexing Terms:
BEHÇET'S DISEASE ETHNIC ORIGIN DISEASE SPECTRUM SEVERITY

Traditionally described as a triad consisting of recurrent aphthous stomatitis, genital ulcerations, and ocular disease, Behçet's disease (BD) is now recognized as a multisystem disorder, the clinical expression of which may be dominated by mucocutaneous, articular, neurologic, urogenital, vascular, intestinal, or pulmonary manifestations[1,2]. Ethnic origin is one of the factors that may modulate the prevalence and expression of BD. It was previously reported that BD has diverse clinical expression in various geographical areas, e.g., the pathergy reaction is considered highly sensitive and specific for BD in patients from Turkey and Japan[1], yet is frequently negative in patients from Western countries[3,4], or gastrointestinal (GI) involvement, which occurs in about one-third of patients from Japan, but rarely in Mediterranean countries. O'Neill, *et al*[5] described regional differences regarding several clinical manifestations of BD. They reported that BD patients from Middle Eastern countries and the Mediterranean basin generally have less widespread disease compared with patients from Western countries (the UK and USA), manifested by lower rates of arthritis, vascular problems, and central nervous system (CNS) abnormalities. Kone-Paut, *et al*[6] found more frequent neurological and GI complications among pediatric patients from France and Saudi Arabia, whereas patients from Turkey had more frequent cutaneous manifestations. We evaluated the influence of ethnic origin on clinical expression and disease severity in Israeli patients.

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MATERIALS AND METHODS

We studied 100 Israeli patients with BD, all of whom fulfilled the International Study Group criteria for BD[7]. There were 66 Jewish and 34 Arabic patients. The 3 largest ethnic groups of Jewish patients originated from Iran/Iraq (n = 21), Turkey (n = 12), and North African countries (n = 21). The other Israeli Jewish patients originated from Yemen (n = 5), Georgia (n = 2), Afghanistan (n = 1), and Ashkenazi Jews (n = 4). Expression of BD was initially compared between Israeli Jewish and Arab patients, and then among the largest Jewish ethnic groups. The following variables were studied: major versus minor oral aphthosis, genital ulcers,

typical skin lesions (erythema nodosum, folliculitis, papulopustular lesions), positive pathergy reaction, ocular disease (anterior uveitis, posterior uveitis or retinal vasculitis), arthritis, vascular disease, CNS disease, GI manifestations, and rate of HLA-B5. Data relating to the entire spectrum of disease manifestations were collected from medical files and patient interviews. The data used for analysis comprises a summation of all the manifestations that have ever occurred in a specific patient.

Major oral ulcers were defined as oral ulcers that are larger than 1 cm in diameter and/or heal with scarring, minor oral ulcers were defined as those smaller than 1 cm that heal without scar formation[8,9].

Severity score was calculated as the sum of 1 point for each mild symptom, 2 points for each moderate symptom, and 3 points for each severe disease manifestation, according to Table 1[9-11].

Statistical analysis. Pearson correlation coefficient (r) and its significance (p) was calculated between the variables. Chi-square test was performed or Fisher's exact test if appropriate to analyze a statistically significant relationship between origin and categorical variables (e.g., sex, HLA, or various clinical manifestations such as genital ulcers, ocular disease, arthritis, etc). Analysis of variance was done using the Duncan multiple comparison option to test statistically significant differences in mean continuous variables (e.g., age at disease onset, disease duration, or severity score) among the groups. p values ≤ 0.05 were considered statistically significant.

RESULTS

One hundred patients were studied, 55 women and 45 men. The mean age of patients was 34.9 ± 11.9 years, disease duration was 13.2 ± 10.2 years, and 72% of patients had HLA-B5. There were no statistically significant differences between Jewish and Arab patients with respect to male:female ratio, prevalence of HLA-B5, age at disease onset, disease duration, or followup periods. Table 2 depicts disease expression in Jewish versus Arab patients. No difference was found between the 2 groups with respect to the rate of major oral ulcers, genital ulcers, ocular disease, skin lesions, positive pathergy reaction, or vascular or neurological involvement. Articular manifestations were somewhat more common in Jewish patients, without reaching statistical significance. Although the overall rate of eye manifestations was similar in the 2 groups, Arab patients had more severe ocular disease, manifested by a significantly higher rate of posterior uveitis (20.6 vs 4.6%; $p < 0.03$). The disease severity score was similar in the 2 groups of patients.

Table 2. Disease expression (%) in Jewish and Arab patients with BD in Israel.

	Jewish Patients n = 63	Arab Patients n = 28	p
Male:female, %	39.4:60.6	55.9:44.1	NS
Age at disease onset, yrs	24.8 ± 14.8	25.3 ± 11.7	NS
Major oral ulcers	35.3	41.7	NS
Genital ulcers	77.3	79.4	NS
Ocular disease	53.0	55.9	NS
Skin lesions	78.8	67.7	NS
Erythema nodosum	36.4	32.4	NS
Pathergy reaction	47.3	36.8	NS
Arthritis	59.1	41.2	0.09
Vascular disease	24.2	26.5	NS
Neuro-Behçet	12.1	14.7	NS
GI involvement	15.9	14.3	NS
HLA-B5	70.4	76.2	NS
Severity score	6.62 ± 2.58	6.38 ± 2.51	NS

Additional comparison of BD manifestations was conducted among the 3 most common Jewish ethnic groups, originating from Iran/Iraq, Turkey, or North African countries (Table 3). The rates of major oral ulcers, genital ulcers, pathergy reaction, and GI involvement were similar in the 3 groups. Although the overall prevalence of skin lesions was similar in the 3 groups, patients originating from Iran/Iraq had a significantly higher rate of folliculitis (61.9 vs 25.0 and 28.6%; $p < 0.05$), while patients of Turkish origin had a lower rate of erythema nodosum (8.3 vs 38.1 and 47.6%; $p = 0.07$). Jewish patients from North African countries had a

Table 1. Severity of Behçet's disease[9–11].

Mild	Oral aphthosis
	Genital ulcers
	Typical skin lesions (erythema nodosum, papulopustular lesions, folliculitis)
	Arthralgia
	Recurrent headaches
	Epididymitis
	Mild gastrointestinal symptoms (chronic diarrhea, chronic abdominal pain)
	Pleuritic pains
	Superficial vein thrombosis
Moderate	Arthritis
	Deep vein thrombosis of the legs
	Anterior uveitis
	Gastrointestinal bleeding
Severe	Posterior/panuveitis, retinal vasculitis
	Arterial thrombosis or aneurysms
	Major vein (vena cava, hepatic) thrombosis
	Neuro-Behçet
	Bowel perforation

Table 3. BD expression (%) in Jewish ethnic groups by region of origin.

	Iran/Iraq n = 21	Turkey, n = 12	North Africa, n = 21	p
Male:female, %	38.1:61.9	33.3:66.6	42.9:57.1	NS
Age at disease onset, yrs	27.5 ± 15.2	19.3 ± 14.5	22.0 ± 13.7	NS
HLA-B5	72.2	75.0	57.1	NS
Major oral ulcers	38.5	40.0	50.0	NS
Genital ulcers	90.5	75.0	66.7	NS
Ocular disease	33.3	41.7	81.0	< 0.01
Total skin lesions	85.7	58.3	81.0	NS
Erythema nodosum	38.1	8.3	47.6	0.07
Folliculitis	61.9	25.0	28.6	< 0.05
Papulopustular rash	14.3	25.0	4.8	NS
Pathergy reaction	57.1	37.5	40.0	NS
Arthritis	52.4	50.0	81.0	0.09
Vascular disease	19.1	8.3	28.6	NS
Deep vein thrombosis	9.5	0	23.8	0.1
Neuro-Behçet	9.5	8.3	23.8	NS
GI involvement	14.3	25.0	19.1	NS
Severity score	5.95 ± 2.77	5.58 ± 1.73	7.81 ± 2.44	< 0.02

significantly higher rate of ocular disease ($p < 0.01$), mainly in the form of anterior uveitis ($p < 0.01$). These patients also had higher rates of arthritis and overall vascular disease as well as deep vein thrombosis and neuro-Behçet, without reaching statistical significance. The disease severity score in this group was significantly higher compared to the other Jewish ethnic groups ($p < 0.02$).

DISCUSSION

Regional variability in disease expression is a well known phenomenon of BD. As there is a broad ethnic heterogeneity of the Jewish population in Israel, we felt our BD population would be suitable for evaluating the effect of ethnic origin on disease manifestations. The results show that the expression of BD is similar in Israeli Jewish and Arab patients. Although joint manifestations were more common in Jewish patients this was not statistically significant. The only difference between the 2 groups was a more severe ocular disease among Israeli Arab patients, manifested by a significantly higher rate of posterior uveitis. Our results are in accord with those of al Aboosi, *et al*, who described ocular involvement of 65% among 20 Jordanian patients with BD, with high proportions (23.1–30.8%) of severe manifestations such as posterior or panuveitis[12]. Similarly, Madanat, *et al* reported a series of 50 Jordanian Arab patients with BD with a high rate (36%) of posterior uveitis[13].

Among the Jewish patients with BD, significantly more severe disease was found in patients originating from North African countries, manifested by a significantly higher rate of ocular disease, mainly in the form of anterior uveitis, as well as higher rates (although not statistically significant) of arthritis, neuro-Behçet, and deep vein thrombosis. The score for disease severity was significantly higher in the patients of North African origin compared to patients originating from Turkey, Iran, or Iraq. The relative expression of BD among different Jewish ethnic groups has not been previously studied. Chajek and Fainaru described the clinical characteristics of 41 patients with BD, of whom 30 were Israeli Jews[14]. In their series, similar rates of ocular, skin, genital, and articular manifestations were reported in patients originating from either North African countries or from Iran/Iraq. Their data, however, may not be comparable to our results, since the selection of patients was based on the very old Curth criteria[15], i.e., 2 symptoms out of aphthous stomatitis, genital ulcers, and uveitis, while our patients were defined according to the International Study Group criteria for BD. Further, the small number of patients in each subgroup (9 patients) is not sufficient to draw clear conclusions regarding ethnic origin and disease manifestations. Our study is the first to provide comprehensive data on the clinical expression of BD among various ethnic groups in Israel. Moreover, we afford an estimation of disease severity with regard to ethnic origin, which may have prognostic implications. According to our results, Jewish BD patients originating from North African countries are at greater risk for more severe disease, especially ocular disease. Awareness of the relationships between ethnic origin and specific clinical manifestations of BD will contribute to our understanding of disease patterns and complications.

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