Epidemiologic and Clinical Survey of Behçet's Disease in Korea: the First Multicenter Study

The prevalence of Behçet's disease is the highest in the East Asian and the Mediterranean countries. Behçet's disease is also distributed in the Asian countries, but the nationwide survey has not been performed in Korea yet. The Korean Study Group for Behçet's Disease, founded in 1999, conducted a multicenter, retrospective survey on epidemiologic and clinical features of the patients with Behçet's disease from 20 hospitals around the nation from 1997 to 1999. Of 3,497 patients, 1,527 were classified into complete or incomplete type of Behçet's disease according to the revised Shimizu's classification. The sex ratio was 1:1.75 with the female predominance. Geographical distribution showed the highest frequency in Seoul (38.5%). Clinically, 98.8% had oral ulcers, 83.2% had genital ulcers, 84.3% had skin lesions and 50.9% had ocular lesions. As for the minor clinical manifestations, articular symptoms were the most frequent. The pathergy test showed positive in 15.4% of patients and revealed a higher positive rate in males (20.2%) than in females (12.7%). In conclusion, we performed the first multicenter study on Behçet's disease in Korea and revealed the female predominance, higher frequency of ocular lesions, and lower positivity of pathergy test in the patients.

Key Words : *Behçet's Disease; Multicenter Studies, Korea*

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INTRODUCTION

Behçet's disease is a chronic systemic inflammatory disease involving mucous membranes, skin, eyes, gastrointestinal tract, joints, vessels, and neurologic systems (1). It occurs endemically in the Middle East and the Mediterranean regions. It is also distributed in the Central and East Asian countries including Korea (2), Japan (3), and China (4). The patients with Behçet's disease have been increasing in Korea and the epidemiological and clinical features of the disease have been reported by some institutes (2). However, the nationwide studies have not been performed yet.

The Korean Study Group for Behçet's disease was founded in 1999 and the first nationwide multicenter survey on epidemiological and clinical features of Behçet's disease in Korea was performed.

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PATIENTS & METHODS

The multicenter study was performed retrospectively with the current data from January 1997 to December 1999. Twenty-four departments from twenty hospitals in Korea participated to this survey. Typical major features including recurrent oral ulcer, skin lesions, eye lesions, and genital ulcers were evaluated in the patients. The patients with four major features diagnosed as complete type, the patients with three major features, two major plus two minor features or typical ocular symptom plus one major or two minor features diagnosed as incomplete type, and the patients with two major features or one major plus two minor diagnosed as suspected type according to the revised Shimizu's classification (5).

A total of 3,497 patients who visited the hospitals in the period were included as having Behçet's disease and were checked by the following inquiry from the hospital records: patient's name, date of birth, sex, geographic distribution, clinical manifestations, durations of the symptoms, and positivity to pathergy test. Durations of symptoms were determined as the period from the beginning of at least one of the diagnostic symptom criteria to the patient's first visit. Geographic distribution was based on the location where the symptom first occurred. Of 3,497 patients, 1,527 fulfilled the Diagnostic Criteria of International Study Group for Behçet's disease (6) and/or the revised Shimizu's classification (5).

Pathergy test was performed with oblique insertion of 26 gauge needle under sterile condition and read by a physician at 24 hr. Formation of papule or pustule was interpreted as a positive result.

Statistical analysis was performed using SPSS version 9.0 (SPSS Inc. Chicago, U.S.A.). Kolmogorov-Smirnov test was applied to evaluate the normality of the age and sex distribution. Chi-square test was applied for comparing the sex difference of pathergy test. Mann-Whitney test was applied to evaluate the age distributions of onset and diagnosis of the disease between males and females. A value of $p<0.05$ was regarded as statistically significant.

RESULTS

Of 3,497 patients, 1,527 were classified as complete or incomplete type of Behçet's disease. According to the Shimizu's classification, incomplete type was the most frequent type (32.8%), followed by suspected type (32.3%), possible type (24.0%) and complete type (10.9%), in order of decreas-
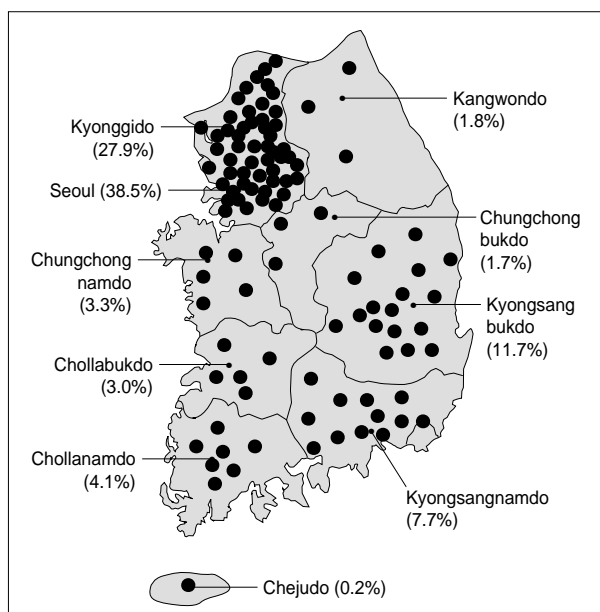
Table 1. Classification of 3,497 patients with Behçet's disease according to the Shimizu's criteria

Classification	Number of patients	%
Complete	382	10.9
Incomplete	1,145	32.8
Suspected	1,130	32.3
Possible	840	24.0

Fig. 1. Geographical distribution of 1,527 patients with Behçet's disease in Korea.

Table 2. Age and sex distributions of 1,527 patients with Behçet's disease

Age (yr)	At the first visit			Age of onset		
	Male	Female	Total (%)	Male	Female	Total (%)
Under 9	0	1	1 (0.07)	5	8	13 (0.85)
10-19	5	8	13 (0.85)	45	79	124 (8.12)
20-29	48	104	152 (9.95)	139	262	401 (26.26)
30-39	181	280	461 (30.19)	217	398	615 (40.28)
40-49	230	396	626 (41.0)	107	161	268 (17.55)
50-59	63	138	201 (13.16)	35	53	88 (5.76)
60-69	28	39	67 (4.39)	8	8	16 (1.05)
Over 70	1	5	6 (0.39)	0	2	2 (0.13)
Total	556	971	1,527 (100)	556	971	1,527 (100)

Table 3. Major and minor symptoms of 1,527 patients with Behçet's disease

Symptoms	Number of patients (%)	Mean duration (months)
Oral ulcers	1,508 (98.8)	93.3
Genital ulcers	1,271 (83.2)	53.8
Skin lesions	1,288 (84.3)	52.9
Ocular lesions	777 (50.9)	42.6
Articular symptoms	586 (38.4)	53.6
Gastrointestinal symptoms	111 (7.3)	58.5
Epididymitis	9 (0.6)	49.7
Vascular symptoms	27 (1.8)	51.4
Neurologic symptoms	70 (4.6)	41.5

Table 4. Result of pathergy test in 715 patients with Behçet's disease

Sex	Number of patients	
	Positive (%)	Negative (%)
Male (n=257)	52 (20.2)	205 (79.8)
Female (n=458)	58 (12.7)	400 (87.3)
Total (%)	110 (15.4)	605 (84.6)

ing frequency (Table 1).

Table 2 summarizes age and sex distributions of the data. The median age of onset was 33 yr (range 1-75) and the median age of diagnosis was 41 yr (range 5-75). The male to female ratio was 1:1.75, indicating female predominance. The age of onset was most commonly in their thirties, followed by twenties (26.3%), forties (17.6%), and teens (8.1%). The age at diagnosis was most commonly in the forties (41%). There was no differences in the age distributions of onset (p=0.444) and diagnosis (p=0.453) of the disease between males and females.

Geographical distribution showed that 38.5% of total patients with Behçet's disease was in Seoul with the highest frequency (Fig. 1). The order of frequencies of geographical distribution was Kyonggido (27.9%), Kyongsangbukdo (11.7%), Kyongsangnamdo (7.7%), Chollanamdo (4.1%), Chungchongnamdo (3.3%), Chollabukdo (3.0%), Kangwondo (1.8%), Chungchongbukdo (1.7%) and Chejudo (0.2%).

Major and minor clinical manifestations are summarized in Table 3 and were oral ulcers (98.8%), skin lesions (84.3%), genital ulcers (83.2%), ocular lesions (50.9%), articular symptoms (38.4%), gastrointestinal symptoms (7.3%), neurologic symptoms (4.6%), vascular symptoms (1.8%), and epididymitis (0.6%), in order of decreasing frequency. The longest mean duration of clinical manifestation was 7 yr and 9 months with oral ulcer.

The results of pathergy test were available in 715 patients with Behçet's disease and showed positive in 110 patients (15.4%) and revealed higher positive rates in males (20.2%) than in females (12.7%) (p=0.008) (Table 4).

DISCUSSION

The prevalence of Behçet's disease is known to be high in Japan, China, Turkey, Tunisia, and the Mediterranean and the Middle Eastern countries. The prevalence of Behçet's disease in Korea also has been reported as high as the countries mentioned above. However, Behçet's disease is rarly

seen in the Northern Europe or in the United States.

The frequency of Behçet's disease in this study demonstrated similar results with the previous report in 1997 performed by Bang et al. with the results as follows (2): complete type 16.1%, incomplete type 38.2%, suspected type 25.4%, and possible type 20.3%.

The result of sexual distribution in our studies was 1:1.75 with the female predominance, which is in line with the previous study. However, in contrast to those studies, Zouboulis et al. (7) reported the male predominance in classical Japanese and Turkish patients with Behçet's disease and yet, there is gradual increase of female patients, which leads to more of 1:1 male-to-female ratio. Saylan et al. (8) also noted the male predominance in almost all middle eastern countries such as Turkey, Iran, Lebanon, Iraq, Jordan, Israel, and Egypt. The countries with the female predominance are Korea, China, the United States and Britain. The difference in sexual distribution among the countries indicates some potential environmental and genetic influences on the pathogenesis of the disease.

The age of onset and the age at diagnosis of Behçet's disease in the present study were slightly older than those in the previous studies. The proprtion of group with the age of onset under 20 was 8.97%, indicating the rarity of Behçet's disease in young ages.

The geographical distribution revealed higher proportion in Seoul and Kyonggido. This result may be due to the differences in the accessibility to the hospitals and population density according to the region. The reports in Japan exhibited a higher prevalence in northern area than southern Japan (9). Nonetheless, our study could not determine distributional differences by the north versus south or by east versus west.

As in other studies, the positive rates of major symptoms revealed that the most frequent major symptom was oral ulcers. As for the minor clinical manifestations, articular symptoms were most frequent. Moreover, the positive rate of ocular lesions in the present study was much higher than that in the previous studies in Korea. The increase in frequency of ocular lesions may be due to the increase in routine tests for the eyes since the ocular lesions are considered to be one of the most important prognostic factors. Furthermore, the exclusion of the possible type in this study might have contributed to the higher frequency of ocular and articular symptoms.

The positivity of the pathergy test in the present study (15.4%) was significantly lower than that of Japan (43.8%) and China (62.2%) (4, 10). This observation may be attributed to the differences in the method of pathergy test or to the racial differences. The positivity of pathergy test is especially high in the Middle Eastern countries, which made the test as a crucial parameter of diagnosis of Behçet's disease. In contrast, the low positive rate of pathergy test in the present study suggests a limitation of its use as a diagnostic criteria in Korea. Yazici et al. (11) reported a higher positive rate of pathergy test in males, which was also observed in the present study.

In conclusion, we performed the first multicenter study on Behçet's disease in Korea and revealed that the female predominance, higher positive rate of ocular lesions and lower positivity of pathergy test were the significant features in Korean patients. Thus, the necessity of close observations on the eyes and further investigation of prevalences through the central registration system should be emphasized.

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