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Behçet's Syndrome in Korea: A Look at the Clinical Picture

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Behçet's syndrome is being detected increasingly in Korea. To collect and document information concerning the clinical picture as it is records of patients seen in our clinic in the period between November 1983 and March 1986 were used as source material. In summary, it was found that (1) the total number of patients who had two major symptoms at least were 410, including 170 men and 240 women; (2) Patients in their thirties were the most common, the mean age being 34.6 years; (3) according to Lehner's classification, the order of frequency of the different types was mucocutaneous (52%), ocular (33), arthritic (14%) and neurologic (1%) and according to Shimizu's classification, it was incomplete (39%), suspected (37%), and complete (24%); (4) oral ulcers, which had observed in 407 patients were the most frequent major symptom, followed by genital ulcers in 338 patients.

Key Words: Behçet's syndrome, clinical picture

Behçet's syndrome is a chronic, systemic disease which manifests itself as recurrent, multiple lesions in many organs, including the skin (Shimizu *et al.* 1979). It was first described by Dr. Hulüsi Behçet in 1937 and is under active research in eastern Mediterranean areas (Dilşen *et al.* 1979; Baserer *et al.* 1979) and Japan.

Although its incidence is known to be high in eastern Mediterranean areas and Asia, especially in Japan, it is distributed worldwide (Shimizu *et al.* 1979). Recently, the number of patients in Korea with Behçet's syndrome detected by dermatologists (Kang *et al.* 1971; Eun *et al.* 1984), ophthalmologists (Park 1973; Lee 1979), and otolaryngologist (Hong *et al.* 1985) has been increasing.

The Behçet's Syndrome Specialty Clinic was opened at Severance hospital in November 1983 as a joint effort of the Department of Dermatology, Ophthalmology, and Otolaryngology. Clinical, immunological, histopathological, electron microscopical, genetic, and therapeutic aspects of the syndrome as it is manifested in the patients registered in the clinic, are under study.

This report is a summary of the statistics on the clinical data of 410 cases which we have able to obtain a sufficient amount of information. Since the patients whose cases were used had at least two major symptoms each, their cases were classified the suspect type, according to Shimizu's classification, and we excluded the cases of 160 patient who had only one major symptom, cases classified as the possible type, according to that classification. And 410 cases were classified according to Lehner's classification.

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SUBJECTS AND METHODS

Subjects

Among the patients who visited our specialty clinic between November 1983 and March 1986, 410 patients who had at least two major symptoms were selected.

Method

Medical records done by dermatology residents according to the guidelines set forth in the study design were reviewed. The symptoms were classified according to Shimizu's classification, the major symptoms included oral ulcers, genital ulcers, eye lesions, and skin lesions, and minor symptoms included arthritic signs, neurologic signs, gastrointestinal signs, and vascular lesions.

RESULTS

Classification

According to Lehner's classification (Lehner and Barnes, 1979) the frequency of the different types was mucocutaneous, 52.2%; ocular, 32.7%; arthritic, 13.9%; neurologic, 1.2%. By Shimizu's classification (Shimizu et al. 1974) it was incomplete, 38.8% and suspect, 37.1%; and complete, 24.1% (Table 1).

Age and sex distribution

Total number of patients was 410 with a male to female ratio of 1:1.4. Patients in their thirties were the most common, followed by those who were in their forties and twenties, with a mean age of 36.5 years (Table 2).

The age of onset was most common in the twenties with a mean age of 29.3 years (Table 3).

Duration of syndrome

The most common duration of 410 cases of

Table 1. Number of patients according to Lehner's and Shimizu's classification

Lehner's Classification				Shimizu's Classification			
Type	Number of patients	% of Total N	M:F Ratio	Type	Number of patients	% of Total N	M:F Ratio
Mucocutaneous	214	52.0	.57	Complete	99	24.1	.94
Arthritic	57	13.9	. 9	Incomplete	159	38.8	.68
Neurologic	5	1.2	.67	Suspect	152	37.1	.57
Ocular	134	32.7	.89	Possible	160*		.47
Total	410	100.0			410		

Mucocutaneous: involves oral and genital ulcer with or without skin manifestation
Arthritic: joint involvement and two or more mucocutaneous manifestation
Neurologic: brain involvement and same or all of lesions found in the mucocutaneous and arthritic types
Ocular: with uveitis and some or all of mucocutaneous, arthritic, and neurologic manifestation
Complete: 4 major symptoms
Incomplete: 3 major symptoms or ocular type and 1 major symptom
Suspect: 2 major symptoms
* Possible: 1 major symptom (excluded in this study)

Table 2. Number of patients, by age and sex

Age (yr) Range	Male (%)		Female (%)		Total (%)	
	Number	% of Total N	Number	% of Total N	N	% of Total N
10 - 19	6	3.6	13	5.4	19	4.6
20 - 29	39	22.9	54	22.5	93	22.7
30 - 39	66	38.8	93	38.8	153	38.8
40 - 49	39	22.9	54	22.5	93	22.7
50 - 59	17	10.0	24	10.0	41	10.0
60 - 69	3	1.8	1	0.4	4	1.0
70 - 79	0	0.0	1	0.4	1	0.2
Total	170	100.0	240	100.0	410	100.0

Table 3. Number of patients, by age of onset and sex

Age (yr) Range	Male (%)		Female (%)		Total (%)	
	Number	% of Total N	Number	% of Total N	N	% of Total N
Under 9	4	2.3	3	1.3	7	1.7
10 - 19	20	11.8	36	15.0	56	13.6
20 - 29	67	39.4	103	42.9	170	41.5
30 - 39	46	27.1	61	25.4	107	26.1
40 - 49	25	14.7	29	12.1	54	13.2
50 - 59	8	4.7	8	3.3	16	3.9
Total	170	100.0	240	100.0	410	100.0

Table 4. Duration, by sex

Duration (years)	Male (%)		Female (%)		Total (%)	
	Number	% of Total N	Number	% of Total N	N	% of Total N
Under 1	16	9.4	29	12.1	45	11.0
1 - 4	73	42.9	70	29.1	143	34.9
5 - 9	46	27.1	77	32.1	123	30.0
10 - 19	26	15.1	53	22.1	79	19.3
20 - 29	8	4.7	9	3.8	17	4.1
Over 30	1	0.6	2	0.8	3	0.7
Total	170	100.0	240	100.0	410	100.0

Table 5. First main symptom to appear

Symptom	Cases	
	Number	%
Oral ulcers	330	80.5
Genital ulcers	30	7.3
Skin lesion	29	7.1
Eye lesions	13	3.2
Joint pain	8	1.9
Total	410	100.0

Table 6. Major and minor symptoms in 410 cases

Symptom	Cases	
	Number	%
Major		
Oral ulcers	407	99.3
Genital ulcers	338	82.4
Skin lesions	301	73.4
Ocular lesion	162	39.5
Minor		
Articular	128	31.2
Neurologic	48	11.7
Gastrointestinal	42	10.2
Vascular	7	1.7

Behçet's syndrome was 1 to 4 years, with a mean duration of 6.4 years (Table 4).

Initial symptoms

Oral ulcer (80.5%) was the most frequent initial symptom of Behçet's syndrome (Table 5).

Major and minor symptoms

Oral ulcers were seen in 407 patients (99.3%), genital ulcers in 82.4%, skin lesions in 73.4%, ocular lesions in 39.5%, articular symptoms in 31.2%, neurologic symptoms 11.7%, gastrointestinal symptoms in 10.2%, and vascular symptoms in 1.7% (Table 6).

We were able to further classify oral ulcers in 407 patients. The minor, major, herpetiform, and combin-

Table 7. Types of oral ulcers in 407 cases

Type*	Cases	
	Number	%
Minor	221	54.3
Major	100	24.6
Herpetiform	11	2.7
Combined	75	18.4
Total	407	100.0

* Minor: 1-5 small and moderately painful ulcers, lasting 4-14 days
Major: 1-10 very painful ulcers, measuring 10-30mm and lasting up to 6 weeks, leaving a scar on healing
Herpetiform: recurrent crops of up to 100 small and painful ulcers

Table 8. Site of oral ulcers in 407 cases

	Cases	
	Number	%
Tongue	324	79.6
Lip	322	79.1
Buccal mucosa	300	73.7
Gingiva	242	59.5
Tonsil	120	29.5
Palate	112	27.5
Pharynx	103	25.3

Table 9. Site of genital ulcers in 183 female cases

Site	Cases	
	Number	%
Vulva	150	82.0
Vaginal mucosa	84	45.9
Groin	18	9.8
Cervix	15	8.2

Table 10. Site of genital ulcers in 155 male cases

	Cases	
	Number	%
Scrotum	107	69.0
Penis	103	66.5
Groin	23	14.8

Table 11. Exacerbation of genital ulcers in relation to menstruation

Stage of Cycle	Cases	
	Number	%
Premenstural	26	55.5
During menstruation	12	25.5
Postmenstruation	9	19.2
Total	47	100.0

Table 12. Types of skin lesions in 301 cases

Skin lesion	Cases	
	Number	%
Erythema nodosum	187	62.1
Papulopustular eruption	171	56.8
Erythema multiforme	21	7.0
Thrombophlebitis	7	2.3
Skin ulcer	7	2.3

Table 13. Relationship to patient of affected members of 55 patients families and their types of the disease

Family number	Number	%	Classification						
			Shimizu			Lehner			
			C	I	S	M	A	N	D
Mother	30	54.5	9	10	11	12	7	2	9
Brother &/or sister	18	32.7	6	8	4	7	3	1	7
Son &/or daughter	16	29.1	3	6	7	9	4		3
Father	10	18.2	0	2	6	7	2		1

C: Complete I: Incomplete S: Suspect
A: Arthritic N: Neurologic O: Ocular
M: Mucocutaneous

Table 14. Distribution of seasonally aggravated symptoms of Behcet's syndrome in 94 patients

Season	Cases	
	Number	%
Spring	26	27.7
Summer	40	42.6
Autumn	15	16.0
Winter	37	39.4

ed types were present in 54.3%, 24.6%, 2.7%, and 18.4% respectively (Table 7).

Frequent sites of oral ulcers were tongue, lips, and buccal mucosa, and genital ulcers were vulva and vaginal mucosa in female; scrotum and penis in male (Table 8, 9, 10).

We studied on the relationship between the genital ulcer and menstrual cycle in female patients with genital ulcers. Forty-seven patients (25.6%) among the 183 female patients with genital ulcers showed aggravation of genital ulcers at some time related to menstruation, most frequently during premenstrual stage (Table 11).

Skin manifestation

Skin lesions were seen in 301 patients. The most frequent symptom was an erythema nodosum-like lesion observed in 187 patients (62.1%); less frequent symptoms, in order frequency of occurence, papulopustular eruption and erythema multiforme like eruption (Table 12).

Family history

A family history was detectable in 55 patients (13.4%). According to the family history, mothers of patients were most frequently affected and siblings, sons were less frequently affected (Table 13).

Seasonal variation

Ninty four patients (22.9%) among the 410 patients with Behçet's syndrome showed seasonal variation in the amount of aggravation of Behçet's syndrome. The symptoms seems to be aggravated more frequent in the spring, summer, and winter and less frequent in fall (Table 14).

DISCUSSION

The fact that the Behçets syndrome is especially prevalent in Japan (Shimizu *et al.* 1979) led us to suspect that a high incidence of the syndrome would also be found in Korea, which shares a geographical, racial, and cultural intimacy with Japan. Past sporadic reports (Kang 1971; Rhim *et al.* 1980; Eun *et al.* 1984; Park 1973; Lee 1973; Hong *et al.* 1985) from in our country supports this hypothesis.

As it may have a severe crippling effect on patients by involving such vital organs as the eyes, vasculature, CNS, and G-I tract, increased awareness and recognition of the syndrome cannot be overemphasized.

The aim of this report is to suggest that the incidence of Behçet's syndrome in Korea is significant, and to present the pattern which the disease follows in its development.

Selection of patients

Most patients were referred from other clinics and all of them (152) were diagnosed in the department of dermatology or the specialty clinic in our hospital as having Behçet's syndorme, because they had at least two major symptoms. Our study included 152 patients with two major symptoms each (the suspect type of Behçet's syndrome), which may have resulted in a lower rate of major entity involvement but otherwise gave more diverse clinical pictures than expected. One hundred and sixty possible type patients, with either recurrent oral or genital ulceration, were excluded from our study due to the difficulty in the differential diagnosis.

Diagnostic criteria and classification

In Lehner's classification of Behçet's syndrome (Lehner and Barnes 1979), based on prognosis, there are the mucocutaneous type and the neurologic-ocular type. In the former the ulcer is associated with pain and discomfort, while in the latter, the symptoms are not severe, but may progress to blindness and death. The authors have seen quite a few cases of the ocular type, and have seen the mucocutaneous type progress to the ocular type, and in view of this, included many mucocutaneous types, even though there are many diseases needing to be differentiated from them. It is very important that the patients be followed up.

We classified the diseases according to the system of classification established by the Behçet's Disease Research Committee of Japan (Shimizu and Inaba 1974). The suspect type, which also must be differentiated from many diseases, is included in this study, since there is a possibility of this type's transforming into a more serious type, and since we wanted to gather more extensive data. On the other hand, we left out the cases which were difficult to differentiate from herpes simplex, simple aphthous ulcer, or erythema multiforme and, also, those difficult to exclude from cases of the mucocutaneous type in which a different final diagnosis might be made.

Sex and age distribution

With a few exceptions in studies from the U.S.A. and Great Britian (Wong *et al.* 1984), most countries,

including Japan, report a male to female ratio of 1-2:1 (Shimizu *et al.* 1979; Dilşon *et al.* 1979; Baserer *et al.* 1979). However, the ratio in our data is 1:1.4, suggesting a greater incidence in females than males.

Previous studies (Eun *et al.* 1984; Lee-1979) which have been carried out in Korea show the same tendency as ours. Nevertheless, there is a tendency for the sex ratio to approach 1 as the disease type gets more severe as in the neurologic-ocular type or complete type. Further studies are needed to determine the sex distribution of the disease in Korea.

The age at the time of diagnosis is known to be most commonly one in the third to fourth decades (Shimizu *et al.* 1979; Dilşon *et al.* 1979; Baserer *et al.* 1979). Our data, in which the same age groups constituted 61.5% of the patients, coincides with this. Also mean age of onset was 29.3 years in our studies as well as in others (Shimizu *et al.* 1979; Dilşon *et al.* 1979; Baserer *et al.* 1979; Wong *et al.* 1984), and similar in either sex. However, the syndrome may appear at both extremes of life, the youngest in our study being a 7-year-old child and the oldest 71-years of age.

Initial symptoms and duration

The most frequent initial manifestation noticed in the patients with Behçet's syndrome was oral ulcers: 80.5% in our study, 73% in Chajek and Fainaru's, 52% in Oshima's, 78% in Lehner's, and 64% in Mason and Bares's.

The interval between the first manifestation and the visit to the clinic varied from a matter of days to matter of years.

Major and minor symptoms

The differences in the selection criteria for patients and the researcher's specialty may be mainly responsible for some inconsistent results among various studies in the past. In our study, of the major four organ involvement, the relative frequency of occurrence of ocular lesions and genital ulcers is somewhat lower than the other studies (Shimizu *et al.* 1979; Dilşon *et al.* 1979; Baserer *et al.* 1979). However, this may be due to relatively large numbers of suspect-type Behçet's syndrome patients, having been included in the study. The lower rate of articular involvement (31.2%) seems also unusual in the light of the report by Mason and Barnes (1969).

The skin

In our study, erythema nodosum was the most frequently observed skin manifestation, followed by papulopustular which included the acneiform eruptions, pustules, and abscesses as in other studies (Shimizu *et al.* 1979; Rhim *et al.* 1980; Eun *et al.* 1984). The incidence of thrombophlebitis was found to be lower. We excluded the needle puncture test because of the next studies for cell-mediated immunity and skin manifestations which were to follow.

Family history

The familial occurrence of Behçet's syndrome has been rarely reported (Lehner 1967; Mason and Barnes 1969). Nevertheless, according to the results of our study, not a small number (13.4%) of the patients had a family history of the disease. Mothers and siblings comprised a great portion of the relatives, while fathers were less often affected.

Seasonal variation

The observation of the seasonal changes in the symptoms revealed that in rather comfortable seasons, such as spring and autumn, the cases in which the symptoms become worse were relatively few in number.

According to the results presented in this study, Behçet's syndrome is rather common in our country, and further studies are needed in order to make possible the classification of the etiology, the pathogenesis, the treatment, and the disease pattern where these are unknown to us at present.

REFERENCES

Baserer T, Mirzatas C, and Basar B: *A clinical study of 147 patients with Behçet's disease.* In Dilşen N, Koniçe M, Ovul C, eds. Behçet's Disease. Amsterdam-Oxford, Excerpta Medica, *1979, 120-123*

Chajek T, Fainaru M: Behçet's desease. Report of 41 cases and a review of the literature. *Medicine 54:179-196, 1975*

Dilşen N, Koniçe M, Ovul C: *Clinical evaluation of 106 cases of Behçet's disease.* In Dilşen N, Koniçe M, Ovul C, eds. Behçet's Disease. Amsterdam-Oxford, Excerpta Medica, *1979, 124-129*

Eun HC, Chung H, Choi SJ: Clinical analysis of 114 patients with Behçet's disease. *J Kor Med Assoc 27:933-939, 1984*

Hong WP, Park IY, Chung MH, Lee JG, Park HJ: Clinical and immunological study on oral lesions of Behçet's syndrome. *Kor J Otolaryn 28:57-62, 1985*

Kang HJ: Behçet's syndrome. *Kor J Dermatol 9:25-30, 1971*

Lee JK: Statiscal study of Behçet's disease. *J Kor Ophth Soc 20:167-174, 1979*

Lehner T: Behçet's syndrome and autoimmunity. *Br Med J*

1:465-467, 1967

Lehner T, Barnes CG: *Criteria for diagnosis and classification of Behçet's syndrome*. In Lehner T and Bares CG, eds. Behçet's syndrome. New York, Academic press, *1979, 1-9*

Mason RM, Barnes CG: Behçet's syndrome with arthritis. *Ann Rhum Dis 28:95-103, 1969*

Oshima Y, Shimizu T, Yokohari R, Matsumoto T, Kano K, Kagami T, Nagaya H: Clinical studies on Behçet's syndrome. *Ann Rheum Dis 22:36-45, 1963*

Park BI: Behçet's disease. *J Kor Ophth Soc 14:114-151, 1973*

Rhim KJ, Choi JS, Son SJ: Clinical observations on Behçet's syndrome. *Kor J Dermatol 18:561-569, 1980*

Shimizu T, Ehrlich GE, Inaba G, Hayasi K: Behçet's disease (Behçet's syndrome). *Sem Arthritis Rheum 8:233-260, 1979*

Shimizu T, Inaba G, Hashimoto T: Diagnostic criteria and their problems of Behçet's disease. *Intern Med 33:278-282, 1974*

Wong RC, Ellis CN, Diaz LA: Behçet's disease. *Int J Dermatol 23:25-32, 1984*