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Cutaneous Manifestations of Behçet's Syndrome

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The clinical features of cutaneous manifestations in 411 patients with Behçet's syndrome were studied. 302 patients (73.5%) had skin lesions. The frequency with which the following skin lesions were noted was, in decreasing order, erythema nodosum-like lesion, papulopustular eruption, erythema multiforme-like lesion, thrombophlebitis, ulcer and Sweet's syndrome-like lesion. More than two types of skin lesions were seen in 86 patients (28.5%), the combination of the skin lesions being, in decreasing order, erythema nodosum-like lesion and papulopustular eruption; erythema multiforme-like lesion and papulopustular lesion; erythema nodosum-like lesion and thrombophlebitis. A skin pathergy test was performed on 245 patients, and a positive reaction was seen in 97 patients (39.6%). This study showed the high incidence, wide spectrum and importance of skin lesions as a major symptom in Behçet's syndrome.

Key Words: Cutaneous manifestation, *Behçet's* syndrome

Since the orginal description of Behçet's syndrome (BS), in 1937 by Behçet (1937), consisting of iritis and recurrent ulcer of the mouth and the genitalia, it is now recognized as a multisystemic disease featuring mucocutaneous, ocular, cardiac, vascular, renal, gastrointestinal, neurologic and/or cutaneous involvement (Shimizu *et al.* 1979).

Various cutaneous lesions which may include erythema nodosum-like lesion, papulopustular eruption, erythema multiforme-like lesion, thrombophlebitis, ulcer, Sweet's syndrome-like lesion and pathergy are frequently seen in BS. Skin lesions are regareded as one of major criteria, only a few reports characterizing the cutaneous manifestations of the disease have been published.

We have reviewed and statistically analyzed the cutaneous manifestations of 411 patients with BS who visited the Behçet's Syndrome Specialty Clinic at Severance Hospital, Seoul, Korea.

PATIENTS AND METHOD

The study included 411 BS patients who visited the Behçet's Syndrome Specialty Clinic of Severance Hospital from November 1983 to March 1986. The patients, 170 male and 241 female (1:1,4), ranged in age from 7 to 71 years with a mean age of 35.6 years. The duration of the disease prior to visiting the clinic ranged from 5 days to 34 years (mean 6.4 years).

Patients were diagnosed using the criteria of Shimizu et al (1974). Major diagnostic criteria included oral ulceration, genital ulceration, eye lesions and skin lesions while minor diagnostic criteria were arthritic signs, neurologic signs, gastrointestinal signs and vascular lesions. A minimum of two major criteria were needed to establish a diagnosis of BS. Data was obtained from hospital records and patient questionnaires.

A skin pathergy test was performed on 245 patients. During the initial visit each patient received an intradermal injection of 0.1 ml normal saline on the skin of the forearm and the appearance of papulovesicular or pustular lesions at the puncture site within 48 hours after puncture was regarded as a positive result.

RESULTS

Age and Sex distribution

Cutaneous involvement was seen in 302 (73.5%) of the 411 BS patients. 133 were male and 169 were female (M:F=1:1.3). Patients in their thirties were the most common, followed by those who were in their twenties and forties, with a mean age of 34.9 years

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Table 1. **Age and sex distribution at the first visit in 302 Behçet's syndrome patients with skin lesions**

Age (years)	Male		Female		Total	
	No. of pts	%	No. of pts	%	No. of pts	%
10 - 19	4	3.0	5	3.0	9	3.0
20 - 29	32	24.1	47	27.8	79	26.2
30 - 39	54	40.6	66	39.0	120	39.7
40 - 49	28	21.1	34	20.1	62	20.5
50 - 59	14	10.5	16	9.5	30	9.9
60 - 69	1	0.7	1	0.6	2	0.7
Total	133	100.0	169	100.0	302	100.0

M: F=1:1.3
Mean age ±SD = 34.9 ± 8.3

Table 2. **Age and sex distribution at the onset in 302 Behçet's syndrome patients with skin lesions**

Age (years)	Male		Female		Total	
	No. of pts	%	No. of pts	%	No. of pts	%
Under 9	3	2.3	2	1.2	5	1.7
10 - 19	15	11.3	28	16.6	43	14.2
20 - 29	53	39.8	71	42.0	124	41.1
30 - 39	37	27.8	44	26.0	81	26.8
40 - 49	20	15.0	19	11.2	39	12.9
50 - 59	5	3.8	5	3.0	10	3.3
Total	133	100.0	169	100.0	302	100.0

Mean age ± SD = 28.8 ± 9.1

(Table 1). Disease onset occured most often during the twenties with a mean age of 28.8 years (Table 2).

Classification

According to the Shimizu's classification, the frequency of the different clinical types in the 302 patients was as followed: incomplete 35.4%; complete 32.8%; suspect 31.8%. Using the Lehner's classification (Lehner and Barnes, 1974) the following frequencies were noted: mucocutaneous 48.7%; ocular 35.1%; arthritic 15.2%; neurologic 1.0% (Table 3).

Cutaneous manifestation

The frequency with with the following skin lesions were noted was, in decreasing order, erythema nodosum-like lesion (Fig. 1), papulopustular eruption (Fig. 2), erythema multiforme-like lesion (Fig. 3), thrombophlebitis (Fig. 4), ulcer (Fig. 5), and Sweet's syndrome-like lesion (Fig. 6) (Table 4). According to the Shimizu's classification, the most common skin lesion of the different clinical types was erythema nodosum-like lesion in the complete and suspect types and papulopustular eruption in the incomplete type (Table 5). By the Lehner's classification, erythema nodosum-like lesion in the mucocutaneous, arthritic and ocular types and papulopustular eruption in the neurologic type occured most frequently (Table 6).

The combination of skin lesion

More than two types lesion were seen in 86 (28.5%) of the 302 BS patients with skin lesions. The combinations of skin lesions were in decreasing order, erythema nodosum-like lesion and papulopustular eruption; erythema multiforme-like lesion and papulopustular eruption; erythema nodosum-like lesion and thrombophebitis; erythema multiforme-like lesion and thrombophlebitis; papulopustular eruption and skin ulcer; and erythema nodosum-like lesion and Sweet's syndrome-like lesion (Table 7).

Skin pathergy test

A skin pathergy test was performed in 245 patients

Table 3. Distribution of 302 of Behçet's syndrome patients with skin lesions according to the classification by Shimizu and Lehner

Clinical type	No. of patients	%
By Shimizu*		
Complete	99	32.8
Incomplete	107	35.4
Suspect	96	31.8
By Lehner**		
Mucocutaneous	147	48.7
Arthritic	46	15.2
Neurologic	3	1.0
Ocular	106	35.1

* Complete ; 4 major symptoms
Incomplete ; 3 majro symptoms or ocular and 1 major symptom
Suspect ; 2 major symptoms

** Mucocutaneous ; oral and genital ulcers with or without skin manifestation
Arthritic ; joint involvement and two or more mucocutaneous manifestations
Neurologic ; brain involvement and some or all of lesions found in the mucocutaneous and arthritic types
Ocular ; uveitis and some or all of mucocutaneous, arthritic, and neurologic manifestations

Table 4. Skin lesions appeared in 302 patients with Behçet's syndrome

Skin lesion	No.	%
Erythema nodosum-like	187	61.9
Papulopustular eruption	163	54.0
Erythema multiforme-like	21	7.0
Thrombophlebitis	7	2.3
Skin ulcer	7	2.3
Sweet's syndrome-like	5	1.7

with a positive reaction (Fig. 7) in 97 patients (39.6%). The positive rate of the pathergy test in 196 patients with skin lesions and 49 patients without skin lesions were 42.4% and 28.6%, respectively. Although the positive rate was higher in the patients with skin lesions than those without skin lesions, there was no significant difference between them (Table 8 & 9).

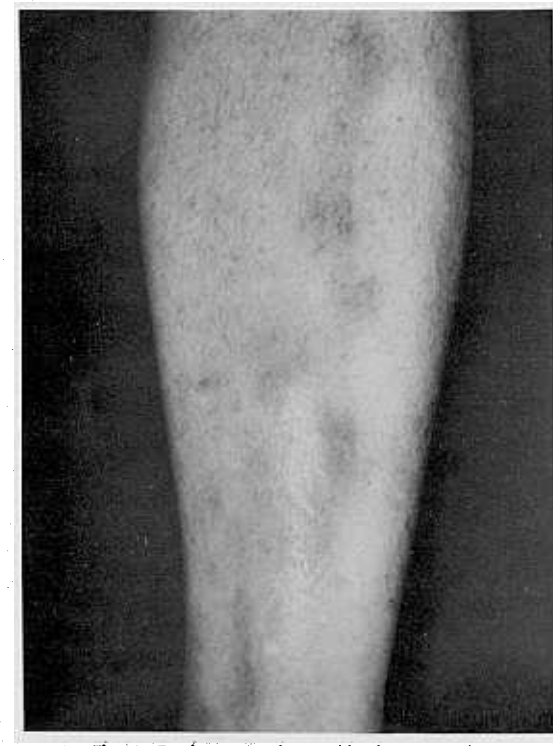

Fig. 1. Erythema nodosum-like lesion on leg.

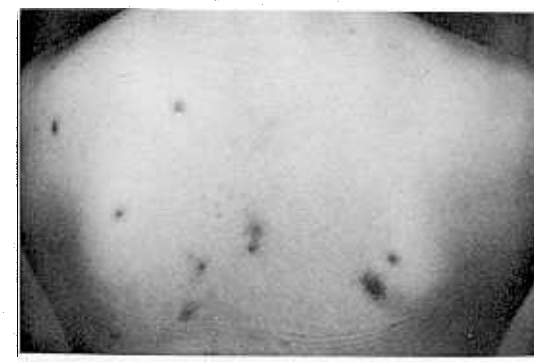

Fig. 2. Papulopustular eruption on back.

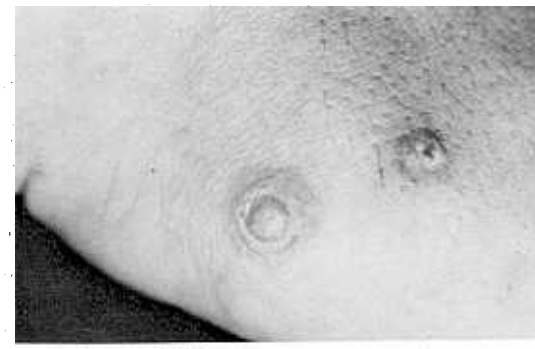

Fig. 3. Erythema multiforme-like lesion on hand.

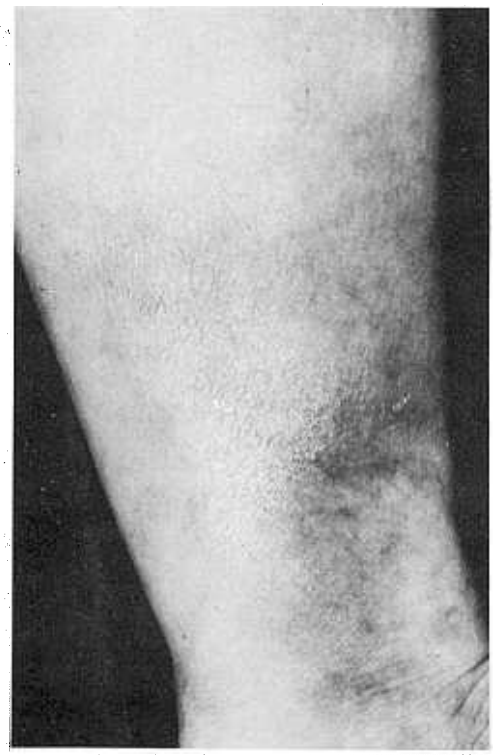

Fig. 4. Thrombophlebitis on leg.

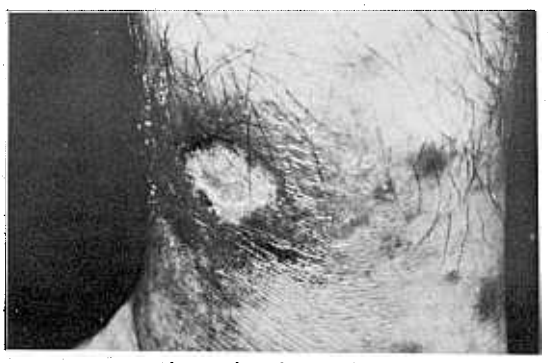

Fig. 5. Skin ulcer on leg.

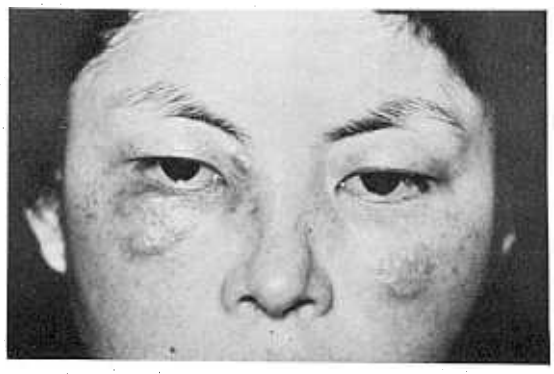

Fig. 6. Sweet's syndrome-like lesion on face.

Table 5. Skin lesions appeared in 302 patients with Behçet's syndrome according to the Shimizu's classification

Skin lesion	Complete (%)	Incomplete (%)	Suspect (%)
Erythema nodosum-like	66 (66.7)	68 (63.6)	53 (55.2)
Papulopustular eruption	47 (47.8)	69 (64.5)	47 (49.0)
Erythema multiforme-like	6 (6.1)	9 (8.4)	6 (6.3)
Thrombophlebitis	3 (3.0)	2 (1.9)	2 (2.1)
Skin ulcer	1 (1.0)	4 (3.7)	2 (2.1)
Sweet's syndrome-like	–	3 (2.8)	2 (2.1)

Table 6. Skin lesions appeared in 302 patients with Behçet's syndrome according to the Lehner's classification

Skin lesion	Mucocutaneous (%)	Arthritic (%)	Neurologic (%)	Ocular (%)
Erythema nodosum-like lesion	96 (65.3)	29 (63.0)	1 (33.3)	61 (57.6)
Papulopustular eruption	90 (61.2)	19 (41.3)	3 (100.0)	51 (48.1)
Erythema multiforme-like lesion	10 (6.8)	4 (8.7)	1 (33.3)	6 (5.7)
Thrombophlebitis	2 (1.4)	2 (4.4)	–	3 (2.8)
Skin ulcer	3 (2.0)	2 (4.4)	–	2 (1.9)
Sweet's syndrome-like lesion	2 (1.4)	2 (4.4)	1 (33.3)	–

Table 7. Number of patients with more than 2 types of skin lesions appeared in 302 patients with Behçet's syndrome

Combination of skin lesions	No. of patients	%
E.N. + P.P.E.	61	20.2
E.M. + P.P.E	9	3.0
E.N. + P.P.E	3	1.0
E.M. + T.P.	3	1.0
P.P.E + Ulcer	3	1.0
E.N. + S.S	2	0.7
P.P.E + S.S.	1	0.3
E.N. + E.M.	1	0.3
E.N. + Ulcer	1	0.3
E.N. + E.M. + P.P.E.	1	0.3
E.N. + P.P.E. + S.S.	1	0.3
Total	86	28.5

E.N. : Erythema nodosum-like lesion
P.P.E. : Papulopustular eruption
E.M. : Erythema multiforme-like lesion
T.P. : Thrombophlebitis
S.S. : Sweet's syndrome-like lesion

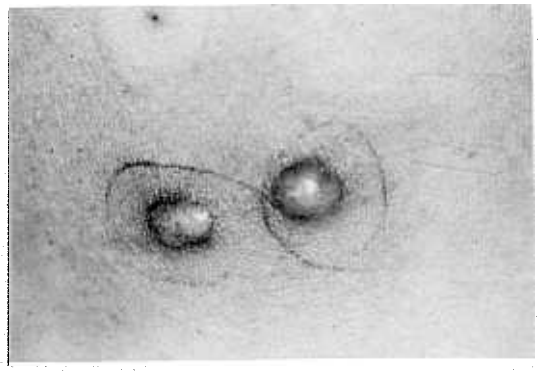

Fig. 7. Positive needle reaction of the skin of a patient with Behçet's syndrome.

Table 8. Result of the skin pathergy test in 245 patients with Behçet's syndrome according to the Shimizu's classification

Clinical type	No. pts positive/No. pts tested (%)	
	with skin lesion	without skin lesion
Complete	31/64 (48.4)	–
Incomplete	33/77 (40.3)	6/12 (50.0)
Suspect	19/55 (34.5)	8/37 (21.6)
Total	82/196 (42.4)	14/49 (28.6)

Table 9. Result of the skin pathergy test in 245 patients with Behçet's syndrome according to the Lehner's classification

Clinical type	No. pts positive/No. pts tested (%)	
	with skin lesion	without skin lesion
Mucocutaneous	37/102 (36.3)	10/31 (32.3)
Arthritic	11/24 (45.8)	2/11 (18.2)
Neurologic	2/29 (100.0)	–
Ocular	33/68 (48.5)	2/7 (28.6)
Total	93/196 (42.4)	14/49 (28.6)

DISCUSSION

This study emphasized the high incidence, wide spectrum and importance of skin lesions as a major symptom in BS. The incidence of cutanceous involvement in BS patients was reported to be 48-88% of patients (Lehner 1977) and in this study, 302 (73.5%) of 411 BS patients had skin lesions.

The prevalance of BS is uncertain. While the disease is most common in Japan, Korea, China and the Middle East (Jorrizo 1986), it is found worldwide (Shimizu *et al.* 1979). Although earlier studies (Shimizu *et al.* 1979; Chajek and Fainaru 1975) suggested that the disease occured more often in men, a recent nationwide survey in Japan (O'Duffy *et al.* 1981) found the male to female ratio to be 0.77:1. Similarly in North America, Britain, and Australiz (Wong *et al.* 1983) women were more frequently affected. In this study the male to female ratio was 1:1.4 in all patients, 1:1.3 in patients with skin lesions.

Although cutaneous manifestations of BS are protean and not characteristic of the disorder except as interpreted in the context of other clinical features, the high incidence of skin lesions makes them a major criterion in the diagnosis of BS. However there is some controversy in including cutaneous follicular or acneiform lesions as a major criterion. Tokoro *et al.* (1977) postulated that the folliculitis essential to BS may be only which occurs in a hair follicle deficient in a sebaceous gland. Jorizzo (1986) postulated that only those lesions documented by neutrophilic vascular reactions or leukocytoclastic vasculitis should be included as skin lesions of BS. In this study, only recurring skin lesions in association with other major symptoms were considered.

The clinical diagnosis of skin lesions in BS is varied. Tokoro *et al.* (1977) classified skin lesions histologically into angiitis, cornium dermatopanniculitis, cornium

dermatitis, and folliculitis or pustular lesions. We classified them clinically as erythema nodosum-like lesion, erythema multiforme-like lesion, Sweet's syndrome-like lesion, thrombophlebitis, cutaneous ulcer and papulopustular eruption including folliculitis, acneiform eruption, papule and pustule. In this study, erythema nodosum-like lesions were the most frequently observed skin lesions, followed by papulopustular eruption as in other studies (Oshima *et al.* 1963; Shimizu *et al.* 1979; O'Duffy *et al.* 1981). However, the incidence of thrombophlebitis was lower than in other studies (Haim 1968; Haim *et al.* 1974). This may be resulted from racial differences.

Skin lesion in any patient may vary in both their macroscopic and histopathologic appearances with the course of the disease, but vascultis is the common denominator (James 1979). In this study, more than two types of skin lesions were found in 28.5% of 302 patients.

The diagnosis of BS primarily depends on the history and clinical findings due to the lack of pathognomic laboratory tests to confirm the suspected clinical diagnosis. Although pathergy only occurs during the active phases of the disease and is evidently only before the initiation of immunosuppressive treatment (Reimer *et al.* 1983), it is very characteristic of BS (Sobel *et al.* 1973). The pathergy test is used as an adjunct to the diagnosis of BS. The mechanism of the phenomenon is not known, but it is thought to be related to an increase in chemotatic activity of polymorphonuclear leukocytes (Matsumura and Mizushima 1975; Djawari *et al.* 1981). We observed a positive pathergy reaction in 39.6% of 245 patients with BS but the positive rate of pathergy in BS was reported to be 40-88% of patients (Tuzun *et al.* 1979; Haim and Gilham 1980). The decreased rate in this study may be due to an inappropriate test time or an inadvertent inclusion of patients who had previously received corticosteroids.

This study assesses the incidence and spectrum of cutaneous manifestations in BS, which with a better understanding of them should aid in the diagnosis of the disease.

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