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Temporal Changes in the Clinical Type or Diagnosis of Behcet's Colitis in Patients with Aphthoid or Punched-Out Colonic Ulcerations

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The intestinal lesion of Behcet's colitis shows aphthoid or punched-out ulceration. However, the diagnosis of Behcet's colitis should be based on the presence of other stigmata of Behcet's syndrome, since these morphological characteristics are not pathognomonic by themselves. Furthermore, the stigmata of Behcet's syndrome could appear simultaneously or separately with intervals of several months to years. Besides, when a physician first meets patients with intestinal ulcerations of aphthoid or punched-out shape, if they do not have any stigma of Behcet's syndrome, the physician has some difficulty in making a diagnosis of Behcet's colitis. The purpose of this retrospective study was to investigate the followings: 1) The upgrade in clinical type of Behcet's colitis with the advance of time. 2) What portion of the patients with aphthoid or punched-out ulcerations, but without any other clinical feature of Behcet's syndrome, could be diagnosed as Behcet's colitis with the advance of time? During the mean follow-up period of 38.2 months, 4 (22.2%) out of 18 patients with Behcet's colitis upgraded their clinical types. In the nonspecific ileocolitis group, who had no major stigma of Behcet's syndrome on their initial visit, 3 (30%) out of 10 patients were subsequently diagnosed as Behcet's colitis during the mean follow-up period of 33.3 months. From these results, we could conclude that in possible or suspicious cases of Behcet's colitis, a more confident diagnosis could be made by close observations for new developments of major stigma of Behcet's syndrome. Even in cases of nonspecific ileocolitis, the diagnosis of Behcet's colitis could be made in a significant number of cases as time goes by.

Key Words: *Behcet's colitis, Aphthoid or punched-out ulceration*

INTRODUCTION

In Behcet's syndrome, if the intestine is involved, the intestinal lesion shows aphthoid or punched-out ulceration (Paik et al., 1986). However, since these morphological characteristics are not pathognomonic by themselves, the diagnosis of Behcet's colitis should be based on the presence of other stigmata of Behcet's syndrome such as orogenital ulcer, skin lesion, or uveitis (Baba et al., 1976; Jung et al., 1984; Lee et al., 1988), and the stigmata of Behcet's syndrome can appear simultaneously or separately with intervals of several months to years (Cho et al., 1988).

When a physician first examines a patient with intestinal ulcerations of aphthoid or punched-out shape, and the patient shows no stigma of Behcet's syndrome, the physician has some difficulty in making a diagnosis of Behcet's colitis. However, our experience showed that if we could follow up such a patient for a long period of time, we would be able to make the diagnosis of Behcet's colitis by newly-appeared major stigma of Behcet's syndrome.

Moreover, in those patients with aphthoid or punched

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out colonic ulcerations in whom we could make a diagnosis of Behcet's colitis on initial presentation because of the presence of some major stigmata of Behcet's syndrome, we noticed that the clinical type of Behcet's colitis could be changed by other newly-appeared major stigma of Behcet's syndrome. To our knowledge, there has been no report with respect to temporal changes in clinical type or diagnosis of Behcet's colitis.

The purpose of this paper was to investigate retrospectively what changes took place in the clinical type of Behcet's colitis over a period and what portion of patients with aphthoid or punched-out colonic ulcerations, but without any other clinical feature of Behcet's syndrome, could be diagnosed as Behcet's colitis over a period?

MATERIALS AND METHODS

Twenty-eight patients with aphthoid or punched-out colonic ulcerations found by colonoscopy were investigated retrospectively from January 1980 to December 1990. Aphthoid ulcer was defined as a shallow ulceration with a discrete margin and grossly normal surrounding mucosa, resembling aphthous ulcer of oral mucosa, and punched-out ulcer as a rather deep clear ulceration with whitish plaque on the ulcer base (Fig. 1). The patients who had caseating granulomas on histological evaluation or acid fast bacilli on tissue smear were excluded. The patients with acute infectious colitis, such as shigellosis and salmonellosis, amoebic colitis, or malignant ulcerations were also excluded from this study.

The diagnosis and classification of clinical types of Behcet's syndrome were made using the criteria proposed by the Behcet's Disease Research Committee of Japan in 1972. If the patient had any major stigma of Behcet's syndrome, then he (or she) was classified into the clinical type of Behcet's syndrome based on the number of major stigma as follows: 1) complete type; those with 4 major stigmata (oral ulcer, genital ulcer, skin lesion, and uveitis), 2) incomplete type; those with 3 major stigmata, 3) suspicious type; those with 2 major stigmata, and 4) possible type; those with 1 major stigma. if the patient did not have any major stigma, then he (or she) was classified as nonspecific ileocolitis despite the presence of the above-mentioned aphthoid or punched-out colonic ulcerations.

In our study, 18 out of 28 patients were classified as Behcet's colitis and the remaining 10 as nonspecific ileocolitis. The mean follow-up periods of these 2 groups were 38.2 months and 33.3 months, respectively (Table 1). During the follow-up period, all patients were analysed very closely for the development of new stigma of Behcet's syndrome in order to investigate the rate of upgrade in the clinical type of Behcet's colitis and the rate of change in diagnosis to Behcet's colitis from nonspecific ileocolitis by new development of the major stigma.

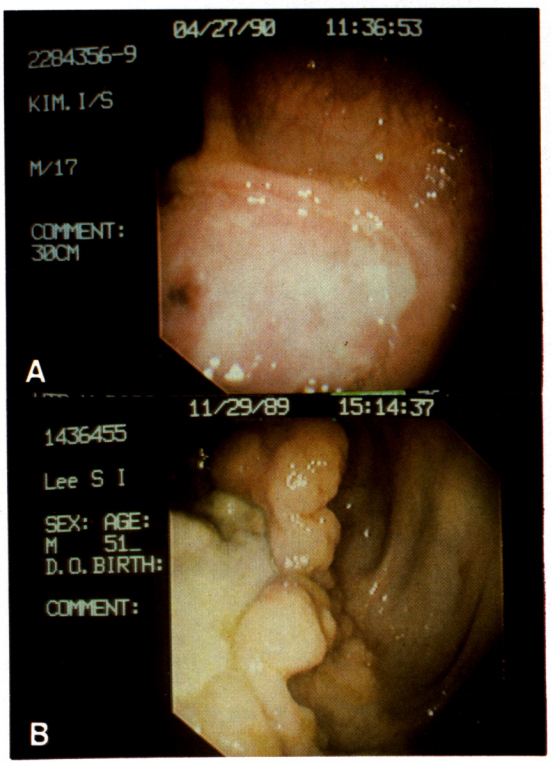

Fig. 1A. A shallow ulcer with discrete margin and grossly normal surrounding mucosa in the cecum shows typical "aphthoid ulcer." Fig. 1B. A rather deep clear ulceration with withish plaque on the ulcer base and somewhat nodular margin represents a "punched-out ulcer" in the cecum.

RESULT

The anatomical distribution of the intestinal lesions in 2 groups is shown in Fig. 2. In both groups most aphthoid or punched-out ulcerations were located proximally, with less common involvement of the distal colon. There was no statistical difference in distribution of the lesions between the 2 groups (Chi-square test, $p > 0.05$).

During the follow-up period, 4 (22.2%) out of 18 patients with Behcet's colitis changed their clinical type as follows: 1 patient from suspicious type to incomplete

Table 1. Profile of patients included in this study

	Behcet's Colitis	Nonspecific Ileocolitis	P-value
No. of patients	18	10	
Age (mean ± SD, yr)	38.3 ± 12.8	38.4 ± 13.9	>0.05
Male/female	14/4	6/4	>0.05
F/U period (mean ± SD, mo)	38.2 ± 34.1	33.3 ± 22.2	>0.05

F/U: Follow-up

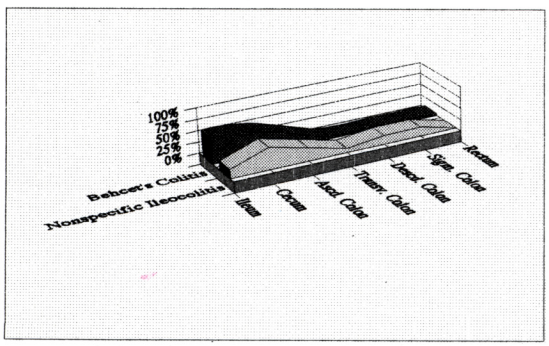

Fig. 2. The anatomical distribution of intestinal lesions in both Behcet's colitis and nonspecific ileocolitis groups. The area means the percentage of involvement for each anatomical location of the colon. No statistical difference of the distribution is shown in both groups (Chi-square test, $p>0.05$).

type, 2 patients from possible type to suspicious type and the remaining 1 patient from possible type, via incomplete type, to complete type (Fig. 3); the details are shown in Table 2. In the nonspecific ileocolitis group, who had no major stigma of Behcet's syndrome on their initial visit, 3 (30%) out of 10 patients were subsequently diagnosed as Behcet's colitis during the follow-up period. 2 patients from nonspecific to suspicious type and 1 patient to possible type (Fig. 4). Table 3 shows the detailed results.

Table 2. Delails of change in involvement of major criteria during a follow-up period in 18 patients of Behcet's colitis.

No. of Cases	Sex/Age	F/U Period (mo)	Major Criteria (initial) OR SK OC GT	Major Criteria (last) OR SK OC GT
1	M/52	45	+ − − −	+ − − −
2	M/29	23	+ − − −	+ − − −
3	F/56	7	+ − + +	+ − + +
4	M/51	14	+ + − +	+ + − +
5	M/39	15	+ − − −	+ − − −
6	M/22	48	+ − − −	+ − − −
7	F/51	51	+ − − −	+ − − +
8	M/24	153	+ − − −	+ + + +
9	F/19	12	+ − − +	+ − − +
10	M/47	9	+ − − −	+ − − −
11	M/31	46	+ + − +	+ + − +
12	M/35	67	+ + − −	+ + − +
13	M/48	41	+ + − +	+ + − +
14	F/32	33	+ − − −	+ − − −
15	M/43	6	+ − − +	+ + − +
16	M/54	55	+ − − −	+ − − +
17	M/41	25	+ − + +	+ − + +
18	M/16	38	+ − − +	+ − − +

OR: oral ulcer, SK: skin lesion, OC: ocular lesion, GT: genital ulcer, F/U: Follow-up

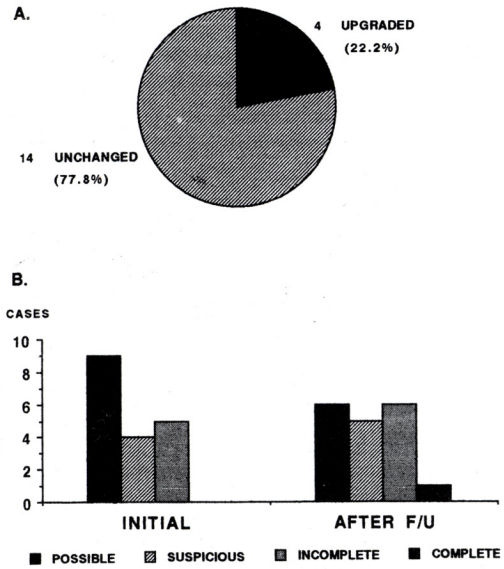

Fig. 3. The upgrade rate of clinical type in the Behcet's colitis group was 22.2% during the mean follow-up period of 38.2 months (A), and the changes are shown in (B).

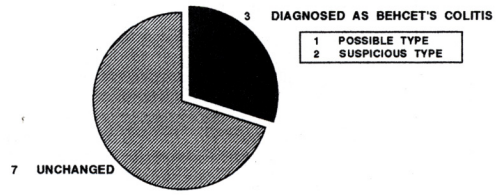

Fig. 4. The diagnostic rate to Behcet's colitis from nonspecific ileocolitis during the mean follow-up period of 33.3 months was 30%. Two patients were diagnosed as suspicious types and 1 was a possible type.

DISCUSSION

Behcet's syndrome was originally described as a triple symptom complex consisting of recurrent orogenital ulcerations and relapsing uveitis. It is now recognized as a multisystem disease that may have mucocutaneous, ocular, intestinal, articular, vascular, urogenital, pulmonary, neurologic, and other features (Shimizu et al., 1979). The disease is more prevalent in Japan, Korea, and Eastern Mediterranean countries (Shimizu et al., 1979) and mainly affects young adults in their third decade (Cho et al., 1988). The overall male-to-female ratio is about 0.6:1 (Cho et al., 1988). In contrast, the male-to-female ratio is 1.7:1 in patients with Behcet's disease with intestinal ulcers (Kasahara et al., 1981).

The diagnosis of Behcet's syndrome may be difficult because of its highly variable clinical presentation and absence of pathognomonic laboratory findings (Shimizu et al., 1979). The diagnostic criteria developed by the Behcet's Disease Research Committee of Japan are shown in Table 4. The diagnosis of Behcet's colitis is challenging especially in the differentiation from chronic inflammatory bowel diseases such as Crohn's disease, ulcerative colitis, and tuberculous colitis in Korea, because the intestinal lesion of Behcet's syndrome has neither pathognomonic gross features nor pathologic findings. Furthermore, the above-mentioned inflammatory bowel diseases could also have extraintestinal manifestations, such as oral aphthous ulcers, ocular, skin, or joint manifestations, mimicking Behcet's syndrome (Rhee et al., 1990). Although the diagnosis of

Table 3. Details of newly-appeared major criteria during the follow-up period in 10 patients of nonspcific ileocolitis group.

No. of Cases	Sex/Age	F/U Period (mo)	Major Criteria (last) OR SK OC GT
1	F/34	18	− − − −
2	M/23	22	− − − −
3	F/37	14	− − − −
4	M/58	34	− − − −
5	M/30	38	− − − −
6	M/54	56	+ − − +
7	M/39	69	− − − −
8	F/56	13	+ − − +
9	M/17	6	+ − − −
10	F/36	60	− − − −

OR: oral ulcer, SK: skin lesion, OC: ocular lesion, GT: genital ulcer, F/U: Follow-up

Table 4. Diagnostic criteria of Behcet's syndrome by Behcet's Disease Research Committee of Japan (1972)

Major Criteria
1. Reccurent aphtous ulceration in the mouth
2. Skin lesions
   a. Erythema nodosum-like eruptions
   b. Subcutaneous thrombophlebitis
   c. Hyperirritability of the skin
3. Eye lesions
   a. Recurrent hypopyon iritis or iridocyclitis
   b. Chrioretinitis
4. Genital ulcerations

Minor Criteria
5. Arthritic symptoms and signs (arthralgia, swelling, redness)
6. Gastrointestinal lesions (appendicitis-like pains, melena, etc.)
7. Epididymitis
8. Vascular lesions (occlusions of blood vessels, aneurysms)
9. Central nervous system involvements
   a. Brain stem syndrome
   b. Meningo-encephalo-myelitic syndrome

Types of Behcet's syndrome
1. Complete type: All 4 major symptoms appear in the clinical course of the patient.
2. Incomplete type:
   a. 3 out of 4 major symptoms appear in the clinical course of the patient.
   b. Recurrent hypopyon iritis or typical chorioretinitis and one other major symptom appear in the clinical course of the patient.
3. Suspicious type: Involvement of 2 major symptoms
4. Possible type: Involvement of only 1 major symptom

Behcet's colitis depends on clinical findings only, it is known that discrete and superficial ulcerations with normal surrounding mucosa and the absence of mucosal friability, so-called "aphthous colitis", could be the characteristic finding of Behcet's colitis (Smith et al., 1973; Eng et al., 1981; Griffin et al., 1982; Nagasako 1982).

The clinical types of Behcet's syndrome are classified mainly by the number of major stigmata, so the higher the number, the more confident the diagnosis. However, the clinical types could be changed temporally, because some mainfestations could appear with the advance of time. A "possible" type of Behcet's syndrome could be changed to "complete" type, if 3 other major criteria newly appeared even after a long time. In one epidemiological study of Behcet's syndrome in Korea, the clinical types of some patients had been changed by newly-developed manifestations after an interval of about 4 to 8 years (Cho et al., 1988).

In our study, 22.2% of the patients with initial diagnosis of Behcet's colitis were upgraded in the clinical type during the mean follow-up period of 38.2 months. In the group with an initial diagnosis of nonspecific ileocolitis, i.e., patients with aphthoid or punched-out colonic ulcerations but without any major stigma of Behcet's syndrome, 30% had the change in diagnosis to Behcet's colitis based on the development of new major stigma during the mean follow-up period of 33.3 months.

From these results, we could conclude that in possible or suspicious cases of Behcet's colitis with rather characteristic findings of aphthoid or punched-out ulcers in the colon, a more confident diagnosis could be made by close observation for new development of major stigma of Behcet's syndrome. Even in cases of nonspecific ileocolitis, if they show such characteristic colonoscopic findings, such as aphthoid or punched-out colonic ulcerations, a diagnosis of Behcet's colitis could be made in a significant number of cases with a period of time based on the development of new

major stigma of Behcet's syndrome.

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