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# Gastrointestinal involvement in Behçet's syndrome: a controlled study

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## Abstract

***Objective*—To make a retrospective and prospective analysis of the frequency of symptomatic inflammatory bowel disease in patients with Behçet's syndrome (BS).**

***Methods*—The medical records of the first 1000 patients with BS were reviewed retrospectively for past or present history of diarrhoea. The past and present history of diarrhoea was also elicited prospectively among 147 consecutive patients with BS and 78 diseased controls (42 with rheumatoid arthritis, 17 with systemic lupus erythematosus, seven with seronegative spondylarthropathy, and 12 with miscellaneous rheumatic diseases). Inflammatory mucosal changes were sought in rectal biopsy specimens from 75 patients with BS, 47 diseased controls (29 with nephrotic syndrome, eight with rheumatoid arthritis, six with familial Mediterranean fever, and four with ankylosing spondylitis), and 14 patients with ulcerative colitis.**

***Results*—In chart review there were only seven Behçet's patients with diarrhoea; none of them had inflammatory bowel disease. In the prospective survey there were no significant differences between the BS and control groups in the past and present history of diarrhoea. There were no significant differences in the rectal mucosal histology between patients with BS and controls, while patients with ulcerative colitis showed pronounced differences.**

***Conclusion*—Symptomatic inflammatory bowel disease is not common in BS patients from Turkey.**


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Since the original description, in 1937, of Behçet's syndrome (BS) as a triple complex of recurrent oral and genital ulcers and uveitis, it has been shown that many organs and systems, including skin, joints, blood vessels, and the gastrointestinal (GI) system, can be affected.[1] The frequency of GI involvement varies in different countries:[1–6] there are several studies, mostly from Japan, reporting a high frequency (50–60%) of GI involvement in BS,[1 2] while a high frequency of GI involvement has not been found among Turkish patients (0–5%) reported as having other disease features.[3 7 8]

We undertook a formal survey of the frequency of inflammatory bowel disease in our patients with BS, using three methods. We reviewed the medical records of the first 1000 Behçet's patients for the presence of diarrhoea, we prospectively elicited a history of diarrhoea among 147 consecutive patients with BS and 78 controls with various rheumatic diseases, and we sought inflammatory mucosal changes in rectal biopsy specimens from 75 patients with BS and 61 diseased controls.

## Patients and methods

### CHART SURVEY

Patients' records held in our multidisciplinary BS outpatient clinic include answers to a question about the presence of diarrhoea at the initial visit. We reviewed the first consecutive 1000 charts among 1800 patients registered at our clinic, for the presence of diarrhoea at the initial visit, and also reviewed the notes from subsequent visits for any references to diarrhoea. At follow up visits, the presence of diarrhoea would have been recorded only if it was mentioned by the patient.

### PROSPECTIVE SURVEY

We prospectively questioned the patients about diarrhoea during an outpatient visit. We asked whether they had experienced any diarrhoea earlier than the preceding three months, within the previous three months, or at any time during their clinic visit. The duration and severity of the diarrhoea and whether it was bloody were also recorded. In this part of the study, 147 consecutive patients with BS and 78 controls with various rheumatic diseases (42 with rheumatoid arthritis, 17 with systemic lupus erythematosus, seven with seronegative spondylarthropathy, and 12 with miscellaneous rheumatic diseases) were screened during their rheumatology outpatient clinic visits. Table 1 gives details of the ages and genders of the patients.

### BIOPSY SURVEY

For this survey, 75 of 99 consecutive rectal biopsy specimens from patients with BS were assessed from a previous study of amyloidosis.[9] Twenty four histological sections were discarded because of poor quality. Although we had not questioned for diarrhoea at the time of biopsy, none of the patients had any history of diarrhoea recorded in their notes. The histological sections of rectal biopsy specimens of 47 patients who had been investigated for the presence of amyloidosis (29 with nephrotic syndrome, eight with rheumatoid arthritis, six with familial Mediterranean fever, and four

*Table 1 Subject details and frequency of diarrhoea among patients with Behçet's syndrome and controls*

| | *Age† (yr)* | *Sex (F/M)* | *Diarrhoea* | | |
|---|---|---|---|---|---|
| | | | *Past§* | *Within 3 months* | *At clinic visit* |
| Behçet's syndrome (n=147) | 33·1 (8·2) | 42/105 | 9 (6)* | 22 (15) | 10 (7) |
| Controls‡ (n=78) | 45·6 (13·5) | 61/17 | 14 (18)* | 11(14) | 4(5) |

Values are †mean (SD) or number (%).
§Earlier than the preceding three months.
*One patient with bloody diarrhoea ($\chi^2 = 6{\cdot}53$; $p < 0{\cdot}02$).
‡42 with rheumatoid arthritis, 17 with systemic lupus erythematosus, seven with seronegative spondylarthropathy, and 12 with miscellaneous rheumatic disease.

*Table 2 Subject details and inflammatory changes in rectal biopsy specimens*

| | *Grades (0–3)* | *Behçet's syndrome (n = 75)* | *Controls§ (n = 47)* | *Ulcerative colitis (n = 14)* |
|---|---|---|---|---|
| Age (years)† | | 35 (9·2) | 39·4 (11·6) | 44·3 (16) |
| Sex (F/M) | | 25/50 | 19/28 | 4/10 |
| Destruction of surface epithelium | 2+3 | 30 (40) | 24 (51) | 14 (100) |
| Lymphoplasmocytic infiltration | 2+3 | 68 (91) | 38 (81) | 14 (100) |
| Polymorphonuclear infiltration | 2+3 | 4 (5) | 6 (13) | 14 (100) |
| Loss of goblet cells | 2+3 | 2 (2) | 5 (11) | 13 (93) |
| Loss of crypts | 2+3 | 5 (6) | 2 (4) | 13 (93) |

Values are †mean (SD) or number (%).
§29 with nephrotic syndrome, eight with rheumatoid arthritis, six with familial Mediterranean fever, four with ankylosing spondylitis.

with ankylosing spondylitis) and 14 patients with ulcerative colitis whose records were selected from the archives of the pathology department were used as diseased controls. Table 2 gives details of the ages and genders of these control subjects.

All specimens were read blind by a pathologist (NT) who graded the following items arbitrarily on a scale from 0 (none) to 3 (severe): destruction of surface epithelium; lymphoplasmocytic infiltration; polymorphonuclear infiltration; loss of goblet cells; loss of crypts.

All patients with Behçet's syndrome fulfilled the International Study Group criteria for this diagnosis.[10]

STATISTICAL ANALYSIS

Statistical analysis was by $\chi^2$ test.

## Results

CHART SURVEY

In 936 of the 1000 medical records (94%), data were available for the presence or absence of diarrhoea. There were six patients (0·006%) (five men and one woman) with diarrhoea that was not described as bloody. Three of these six patients with a history of intermittent diarrhoea during their first visits were free of this symptom during their follow up period, which ranged from four to nine years. One patient was offered further investigation of his diarrhoea, but he refused and was lost to follow up. Another patient had a normal barium enema of the large bowel and was found to have giardia intestinalis infestation. A third patient underwent sigmoidoscopy, a barium enema of the large bowel, and two colon biopsies; all were within normal limits. Finally, a female patient complained of intermittent diarrhoea after a follow up of three years; a rectoscopic examination was normal and she responded to amitriptyline.

PROSPECTIVE SURVEY

Table 1 shows that the frequency of a history of diarrhoea was generally similar in patients with BS and diseased controls, but was lower in the group with BS for the period earlier than the preceding three months. When present, the diarrhoea never lasted more than 10 days. In one patient in each group it was bloody, but was of short duration.

BIOPSY SURVEY

Table 2 gives the findings of biopsy specimens. When moderate and severe grades (grades 2 plus 3) were taken together, there were no significant differences between patients with BS and the controls. In contrast, the patients with ulcerative colitis had pronounced pathology.

## Discussion

GI involvement in Behçet's syndrome may affect all areas from the lips to the anus.[11] The ulcers are most commonly found in the terminal ileum and the caecum (75% of patients) and less frequently in the colon, sparing the rectum (3%) in contrast to the pathology in ulcerative colitis. Multiple deep, flask shaped ulcers in the presence of chronic non-specific, but sometimes granulomatous, inflammation and normal intervening mucosa are characteristically seen on histopathological examination.[1 12] However, focal colitis in rectal biopsy specimens in asymptomatic patients from Turkey has also been described.[13] Therefore, in addition to our clinical survey for the presence of diarrhoea as an indicator of inflammatory bowel disease among our patients, we also undertook a controlled, blinded study of rectal biopsy specimens.

It was notable from our questionnaire that there was no difference in the frequency of diarrhoea within the previous three months and at the time of the clinic visit (table 1). We do not have an explanation for the unexpected lower frequency of diarrhoea noted among the Behçet's patients seen during the period earlier than the preceding three months ($\chi^2 = 6{\cdot}53$, $p < 0{\cdot}02$), though it may have been the result of underrecording of diarrhoea in the patients' charts. Alternatively, patients with diarrhoea may have sought medical attention elsewhere, with the result that we subsequently observed a lower frequency of diarrhoea in this group. These two potential biases arising from the retrospective part of the study must be taken into consideration in interpreting our results. Furthermore, while we did not find inflammatory changes of either moderate or severe degree in rectal biopsy specimens from patients with Behçet's syndrome, it is certainly possible that some of our patients may have had asymptomatic lesions at locations in the GI tract that we did not examine.

The results of this study in general parallel our earlier observation that, as judged by the symptom of diarrhoea, symptomatic inflammatory bowel disease is at best infrequent in Turkish patients with BS. This is in contrast to findings in Japan, where a high frequency (50–60%) of patients with BS were reported to have symptoms of inflammatory bowel disease such as diarrhoea, abdominal pain, and abdominal distension.[1 2] There are also several case reports of similar GI involvement in Behçet's syndrome, including a case in a child.[14] However, in a well described series of 41 patients from Israel, no GI symptoms apart from oral aphthae were reported.[4] In the United Kingdom, three of 32 patients had gastrointestinal involvement, one of whom had proven Crohn's disease,[5] and three of 10 patients reported from the USA had chronic colitis.[6] Among 150 patients attending a surgical department at Ankara, Turkey, seven patients with involvement of the terminal ileum and the ileocaecal area required surgery,[8] but we have found superficial ulcerations in the ileocaecal area in only one case among seven postmortem examinations in patients with BS who died from causes not related to GI (unpublished observations).

Geographical differences in the features of BS are not confined to the GI tract. A high frequency (about 80%) of both pathergy test positivity and HLA-B5 were encountered in patients from Japan and the Mediterranean countries including Turkey, in contrast to patients in the United Kingdom and the USA.[15] These variations in disease expression remain to be explained in this syndrome of unknown aetiology.


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