

## 전체 위장관을 침범한 베체트 장염 환자에서 연속 발생한 위, 결장 천공

연세대학교 의과대학 내과학교실, 소화기병연구소\*, 외과학교실<sup>†</sup>, 병리학교실<sup>‡</sup>

신동엽 · 천재희\* · 박재준\* · 김호근<sup>‡</sup> · 김태일\* · 이용찬\* · 김남규\*<sup>†</sup> · 김원호\*

### Serial Episodes of Gastric and Cecal Perforation in a Patient with Behcet's Disease Involving the Whole Gastrointestinal Tract: A Case Report

Dong Yeob Shin, M.D., Jae Hee Cheon, M.D.\*, Jae Jun Park, M.D.\*, Hoguen Kim, M.D.<sup>‡</sup>, Tae Il Kim, M.D.\*, Yong Chan Lee, M.D.\*, Nam Kyu Kim, M.D.\*<sup>†</sup>, and Won Ho Kim, M.D.\*

Department of Internal Medicine and Institute of Gastroenterology\*,  
Departments of Surgery<sup>†</sup> and Pathology<sup>‡</sup>, Yonsei University College of Medicine, Seoul, Korea

Behcet's disease (BD) has been recognized as multi-systemic chronic vasculitic disorder of recurrent inflammation, characterized by the involvement of multiple organs and resulting in orogenital ulcers, uveitis, and skin lesions. Involvement of the central nervous system, vessels, and intestines in BD often leads to a poor prognosis. Digestive manifestations in BD have been reported in up to 1-60% of cases, although the rate varies in different countries. The most frequent extra-oral sites of gastrointestinal involvement are the ileocecal region and the colon. Gastric or esophageal involvement is reported to be very rare. Moreover, there have been no reports on the simultaneous involvement of the esophagus, stomach, ileum, and colon. Here, we present a 55-year-old Korean man with intestinal BD and multiple ileal and colonic ulcerations complicated by perforation, gastric ulcer with bleeding followed by perforation, and esophageal ulcers with bleeding. (**Korean J Gastroenterol 2009;53:106-110**)

**Key Words:** Behcet's disease; Gastrointestinal; Ulcer; Perforation; Hemorrhage

### Introduction

Behcet's disease (BD) is a chronic multi-systemic vasculitis characterized by recurrent oral, genital aphthae, and ocular disease. Although the cause is unknown, the presumptive etiologies of BD include infections, autoimmune, and genetic mechanisms.<sup>1</sup> The prevalence of this disease differs widely among countries; while the rate is 0.3/100,000 in the United States, it is 1/10,000 in Japan.<sup>2</sup> The syndrome can cause

dysfunction in multiple organ systems, leading to conditions such as myocarditis, aneurysm, pulmonary thromboembolism, central nervous system abnormalities, renal involvement, and gastrointestinal manifestations.<sup>3,4</sup> Gastrointestinal manifestations have been known to lead to severe morbidity in BD patients and are commonly referred to as "Intestinal Behcet's syndrome". The terminal ileum and the cecum are the most frequently involved parts of the gastrointestinal tract and gastric or esophageal involvement is very rare. Esophageal involvement has been reported in less than 50 cases of BD with esophageal

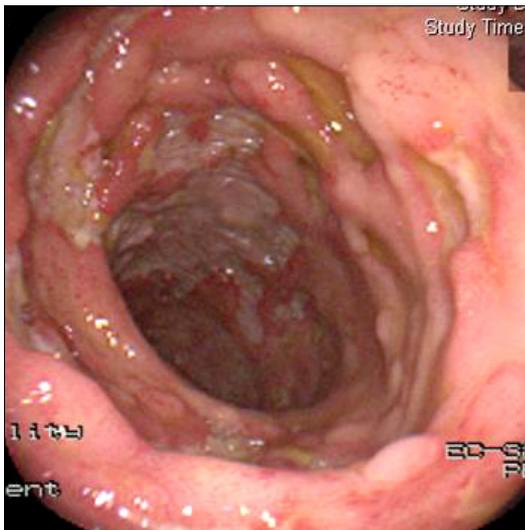
접수: 2008년 7월 3일, 승인: 2008년 9월 16일  
연락처: 천재희, 120-749, 서울시 서대문구 신촌동 134  
연세대학교 의과대학 내과학교실  
Tel: (02) 2228-1990, Fax: (02) 393-6884  
E-mail: geniushee@yuhs.ac

Correspondence to: Jae Hee Cheon, M.D.  
Department of Internal Medicine and Institute of Gastroenterology, Yonsei University College of Medicine, 134, Shinchon-dong, Seodaemun-gu, Seoul 120-752, Korea  
Tel: +82-2-2228-1990, Fax: +82-2-393-6884  
E-mail: geniushee@yuhs.ac

ulcers worldwide.<sup>5</sup> Furthermore, gastric involvement is extremely rare, with an incidence lower than that of esophageal BD.<sup>6</sup> There have not been any reports on simultaneous esophageal, gastric, ileal, and colon involvement. Here, we report a 55-year-old Korean man with intestinal BD and multiple ileal and colonic ulcerations complicated by perforation, gastric ulcer bleeding followed by perforation, and esophageal ulcers with bleeding.

### Case Report

A 55-year-old man was admitted to the emergency department for abdominal pain for 3 months. He had a past history of receiving a coronary angiography for the evaluation of chest pain 8 years prior, but it failed due to severe stenosis of both common iliac arteries and both subclavian arteries. A diagnosis of peripheral arterial occlusive disease was made, then an aorto-left common femoral artery bypass graft and femoro-femoral artery bypass graft and stent insertion at both subclavian arteries was performed. He had been taking anti-platelet agent, aspirin 100 mg per oral and anti-hypertensive agents since 8 years ago. He also had been suffered from recurrent oral and genital ulcers for the previous 5 years. Three months before visiting our hospital, he had been admitted to a primary clinic and had undergone esophagogastroduodenoscopy (EGD) and colonoscopy, which revealed ileocolonic ulcers (Fig. 1). He was referred to our hospital because there had been no improvement in symptom after steroid treatment

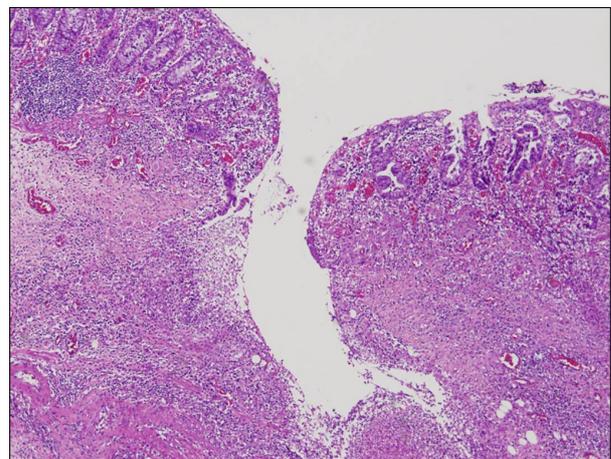


**Fig. 1.** The colonoscopic finding shows multiple and discrete ulcers in the ascending colon.

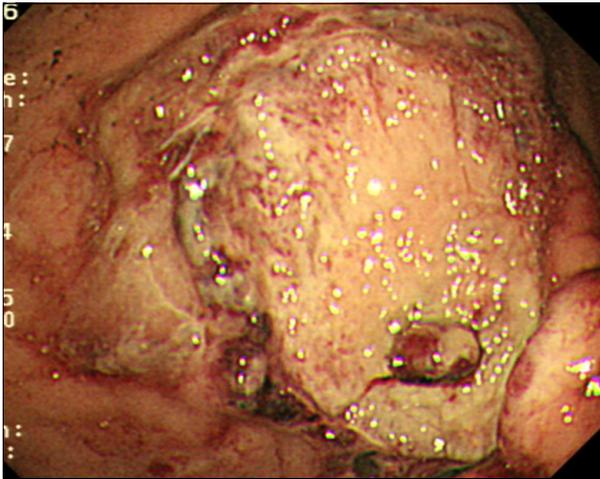
with the impression of Crohn's disease.

On admission, the patient's vital signs were stable. Although he complained of diffuse abdominal tenderness, there was no rebound tenderness or rigidity. He had well-demarcated, punctuated oral and genital ulcers suggesting BD. Uveitis was not seen on eye exam. Pathergy test was negative. Laboratory values showed a white blood cell count of 32,200/ $\mu$ L, hemoglobin of 13.1 g/dL, a platelet count of 174,000/ $\mu$ L, and an ESR of 14 mm/hr. His liver function test was normal and CRP was 12.7 mg/dL. Anti-cytomegalovirus IgM and anti-amebic IgM antibodies were negative. Although he didn't have fever on admission day, he developed a fever of 38.1°C on his second day of admission.

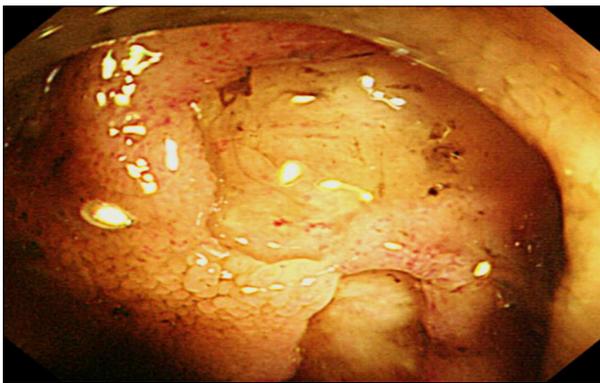
His abdominal pain and fever were not improved despite 4 days of antibiotics therapy. Abdominal CT scan showed active inflammation with diffuse wall thickening at the cecum, ascending colon, and transverse colon. Abdominal pain was aggravated and he had newly developed hematochezia. On physical examination, rebound tenderness of whole abdomen became obvious. Accordingly, he underwent emergent right hemicolectomy with ileostomy with suspicion of intestinal perforation. The operation revealed two sites of intestinal perforations from the cecum to the ascending colon. Microscopic examination of the specimen showed transmural inflammation, discrete ulcer margins, and no chronic surrounding mucosal change, suggestive of intestinal BD (Fig. 2). Other types of colitis such as viral or neoplastic diseases were excluded by immunohistochemistic staining. Seven days after the operation, the patient had a large amount of melena. An



**Fig. 2.** Microscopic finding of the surgical specimen shows multiple ulcer perforations with diffuse inflammation in the cecum and ascending colon (H&E stain,  $\times$ 200).



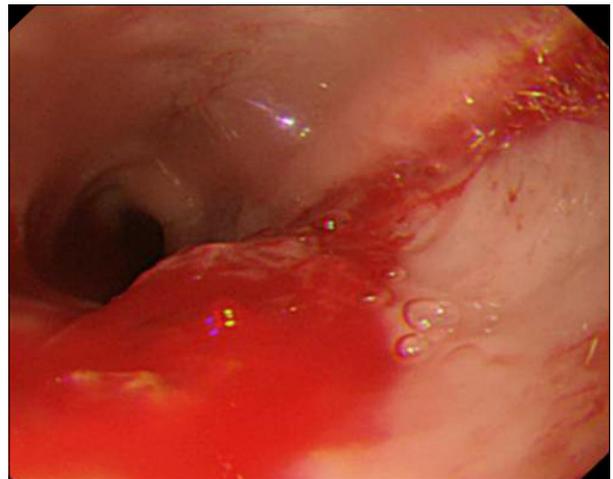
**Fig. 3.** Esophagogastroduodenoscopic finding shows an active ulcer with mucosal edema in the lesser curvature of the lower body in the stomach. There is a bleeding stigmata with vessel exposure at the base of the ulcer.



**Fig. 4.** Ileoscopic examination showing the active ulcer at 8 cm from the ileostomy site. There is no evidence of recent bleeding.

emergency EGD showed an oval-shaped active ulcer with a discrete margin in the lesser curvature of the lower body in the stomach. There was a stigmata of recent bleeding (Fig. 3). Thereafter, melena was spontaneously subsided. On postoperative day (POD) 25, he was discharged with daily doses of 3 g of mesalazine and 30 mg of prednisolone per oral with the diagnosis of intestinal BD involving stomach and ileocolon.

Twelve days after discharge, the patient was admitted again due to severe abdominal pain. Emergent laparotomy revealed panperitonitis with gastric ulcer perforation. Genital and oral ulcers developed again on PODs 7 and 14, respectively. On POD 19, he had hematochezia. Enteroscopy through the ileostomy site showed no evidence of recent bleeding, but



**Fig. 5.** Esophagoscopy finding shows two esophageal ulcers with current bleeding at 25 cm from the incisors.

revealed an ileal ulcer (Fig. 4). However, he had a large amount of melena again on POD 28. Whereas abdominal aortography revealed no bleeding focus, EGD showed two discrete esophageal ulcers with a bleeding vessel at 25-30 cm from upper incisor (Fig. 5). After hemoclippping, the bleeding was stopped. His further postoperative course was uneventful, and the patient was followed-up without any further episode of hemorrhage. After being discharged, he was prescribed 50 mg of azathioprine, 30 mg of prednisolone, and 1.8 mg of colchicine.

## Discussion

BD was first described in 1937 by Turkish dermatologist, Hulusi Behcet as a triple complex of chronic, recurrent oral and genital ulcers, and uveitis. The underlying cause of BD is still unknown and the diagnosis is mainly based on the clinical features.<sup>1,7</sup> Several sets of criteria had been employed to diagnose and classify BD. In 1990, the international study group (ISG) introduced a new, internationally agreed upon criteria for BD based on a survey of 913 patients recruited from 12 centers in 7 countries. The ISG criteria requires the presence of recurrent oral ulceration plus any two of genital ulceration, typically defined eye lesions, skin lesions, or a positive pathergy test.<sup>8</sup> The oral and genital ulcers were found during the initial physical examination of this patient. In addition, the patient's multiple arterial occlusions and coronary artery occlusive diseases that had developed recurrently for 8 years are thought to be related to the vascular involvement of

BD. Large vessel involvement is known to occur in one-third of the patients with BD. Arteries and veins of all sizes can be affected and arterial complications are less common than venous problems in BD, occurring in roughly 1-7% of patients. Male sex and cigarette smoking are known risk factors.<sup>9</sup> His manifestations do not fully satisfy the ISG criteria, but do fulfill two of the main and two of the minor diagnostic criteria for BD proposed by the BD Research Committee of Japan and can be categorized as "incomplete type" BD.<sup>10</sup>

The frequency of intestinal involvement in patients with BD is known to be 0-60%, with geographic differences.<sup>11</sup> Symptomatic intestinal involvement is rare in Mediterranean patients with BD, but in East Asian patients, including Koreans, intestinal involvement is more common.<sup>12,13</sup> The intestinal lesions are usually resistant to medical treatment and recur frequently (25-78%) after surgical management.<sup>14</sup> Intestinal BD with gastrointestinal ulcer is reported to account for only 1% of cases in Western countries. In contrast, Asian patients with BD tend to experience intestinal ulcer more frequently. The main symptoms include anorexia, nausea, abdominal pain, and diarrhea.<sup>13</sup> Large, discrete, punched-out-appearing ulcers are characteristics of intestinal BD. Fistula formation, hemorrhage, or perforation occurs in up to 50% of ulcers in BD.<sup>15</sup> The most common location of involvement is the ileocecal region (60-75%).<sup>16</sup> So far, only nine cases of intestinal Behcet's disease presenting with both esophageal and ileocolonic ulcers have been reported in the English literature.<sup>2</sup> The gastroduodenal mucosa is known to be the least frequently involved area of the gastrointestinal tract, although Ning-Sheng et al. reported a relatively high prevalence of gastric/duodenal ulceration in patients with BD in Taiwan.<sup>6</sup> Recently, Isik et al. reported three cases of intestinal perforations in patients with BD. These patients underwent the operations two to four times. The reasons for re-operation were ulcer perforation after primary repair, or postoperative complications like fistula and leakage.<sup>17</sup> To our knowledge, there has been no case report of simultaneous involvement of the esophagus, stomach, ileum, and colon with multiple intestinal perforations in BD. Ulcerogenic medications like aspirin or steroids and the severe stress might have been aggravating factors for the BD associated ulcer rather than direct causes, considering relatively long duration of taking aspirin without ulcer event, refractoriness to conventional anti-ulcer treatment, and normal finding of previous EGD performed in other hospital.

In conclusion, we present an exceptionally rare case of

intestinal BD involving the whole gastrointestinal tract and leading to recurrent hemorrhage and ulcer perforation. Although rare, intestinal involvement of BD can lead to very severe complications and can involve multiple sites concurrently. The evaluation of the whole gastrointestinal tract may be necessary in BD patients who develop intestinal symptoms.

## References

1. Ghatge JV, Jorizzo JL. Behcet's disease and complex aphthosis. *J Am Acad Dermatol* 1999;40:1-18.
2. Fujiwara S, Shimizu I, Ishikawa M, et al. Intestinal Behcet's disease with esophageal ulcers and colonic longitudinal ulcers. *World J Gastroenterol* 2006;12:2622-2624.
3. Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. *N Engl J Med* 1999;341:1284-1291.
4. Koc Y, Gullu I, Akpek G, et al. Vascular involvement in Behcet's disease. *J Rheumatol* 1992;19:402-410.
5. Morimoto Y, Tanaka Y, Itoh T, Yamamoto S, Kurihara Y, Nishikawa K. Esophagobronchial fistula in a patient with Behcet's disease: report of a case. *Surg Today* 2005;35:671-676.
6. Ning-Sheng L, Ruay-Sheng L, Kuo-Chih T. High frequency of unusual gastric/duodenal ulcers in patients with Behcet's disease in Taiwan: a possible correlation of MHC molecules with the development of gastric/duodenal ulcers. *Clin Rheumatol* 2005;24:516-520.
7. Mutlu S, Scully C. The person behind the eponym: Hulusi Behcet (1889-1948). *J Oral Pathol Med* 1994;23:289-290.
8. Criteria for diagnosis of Behcet's disease. International Study Group for Behcet's Disease. *Lancet* 1990;335:1078-1080.
9. Calamia KT, Schirmer M, Melikoglu M. Major vessel involvement in Behcet disease. *Curr Opin Rheumatol* 2005;17:1-8.
10. Suzuki Kurokawa M, Suzuki N. Behcet's disease. *Clin Exp Med* 2004;4:10-20.
11. Yurdakul S, Tuzuner N, Yurdakul I, Hamuryudan V, Yazici H. Gastrointestinal involvement in Behcet's syndrome: a controlled study. *Ann Rheum Dis* 1996;55:208-210.
12. Shimizu T, Ehrlich GE, Inaba G, Hayashi K. Behcet disease (Behcet syndrome). *Semin Arthritis Rheum* 1979;8:223-260.
13. Oshima Y, Shimizu T, Yokohari R, et al. Clinical studies on Behcet's syndrome, with special reference to 100 personal cases. *Naika* 1962;9:701-714.
14. Iida M, Kobayashi H, Matsumoto T, et al. Postoperative recurrence in patients with intestinal Behcet's disease. *Dis Colon Rectum* 1994;37:16-21.

15. Jarrahejad P, Gadepalli S, Zurkovsky E, Tulsyan N, Rolandelli R. Behcet's disease: a rare cause of lower gastrointestinal bleeding. *Int J Colorectal Dis* 2006;21:856-858.
  16. Kasahara Y, Tanaka S, Nishino M, Umemura H, Shiraha S, Kuyama T. Intestinal involvement in Behcet's disease: review of 136 surgical cases in the Japanese literature. *Dis Colon Rectum* 1981;24:103-106.
  17. Isik B, Ara C, Kirimlioglu H, et al. Single or multiple perforations with varying locations as a complication of intestinal Behcet's disease: report of three cases. *Scand J Gastroenterol* 2005;40:599-603.
-