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The risk of ileocolonic perforation in patients with Behçet's Disease: A Report of three cases and a review of the literature

Behçet'lilerde ileokolonik perforasyon riski: Üç olgu sunumu ve literatürün gözden geçirilmesi

Mehmet BEKTAŞ[1], Çağdaş KALKAN[1], İrfan SOYKAN[1], Ayşe BOYVAT[2], Berna SAVAŞ[3], Ethem GEÇİM[4], Onur KESKİN[1], Ekin KIRCALİ[1], Ali TÜZÜN[1], Necati ÖRMECİ[1]

Departments of [1]Gastroenterology, [2]Dermatology, [3]Pathology and [4]General Surgery, Ankara University School of Medicine, Ankara

Background and Aims: *Intestinal Behcet's disease may cause serious complications, including massive hemorrhage, fistulisation and intestinal perforation, which are encountered in approximately 50% of patients. Currently, there is little data on iatrogenic ileocolonic perforation during colonoscopy in patients with intestinal Behcet's disease; therefore, our aim is to perform a retrospective review of records of intestinal Behcet's disease patients who suffered perforation during or after colonoscopy.* ***Materials and Methods:*** *A total of 2615 colonoscopic examinations were performed between May 2002 and December 2007. The main indication for colonoscopy was intestinal Behcet's disease in 135 of the 2615 patients.* ***Results:*** *135 patients with Behcet's disease were evaluated by colonoscopy due to presumed ileocolonic involvement. Eight out of 135 (5.9%) patients had ileal and colonic ulcers. 3 patients (2.22%) had iatrogenic perforation; 2 of whom had profound ulcers in proximal colon and ileum. The third case had ulcers in the sigmoid, descending and transverse colon segments. All 3 patients had undergone surgical intervention that included ileal resection and right hemicolectomy.* ***Conclusion:*** *Colonoscopic examination is commonly used in Behcet's disease not only for diagnostic purposes but also for surveillance of intestinal involvement. Volcano-shaped ulcers are especially prone to perforate. Both clinicians and endoscopists should be alert against barotrauma during colonoscopy since it may cause perforation. Patients should also be followed, and in case of abdominal pain after colonoscopic examination, colonic perforation should be considered.*

Key words: *Behcet's disease, colonoscopy, ileocolonic perforation*

Giriş ve Amaç: *İntestinal Behçet Hastalığı ciddi komplikasyonlara neden olabilir. Masif kanama, fistülizasyon ve intestinal perforasyon, intestinal Behçet Hastalığı olanların yaklaşık %50'sinde rastlanan komplikasyonlardır. İntestinal Behçet tanısı alanlarda, kolonoskopi sırasındaki iatrojenik ileokolonik perforasyonu inceleyen yeterli çalışma ve data yoktur. Bu nedenle biz intestinal Behçet Hastalığı olanlarda kolonoskopi sırasında ve kolonoskopi sonrasında gelişen perforasyon sorununu incelemeyi amaçladık.* ***Gereç ve Yöntem:*** *Mayıs 2002 ile Aralık 2007 tarihleri arasında üniversitemizde yapılan 2615 kolonoskopi olgusu değerlendirildi. Bu 2615 olgunun 135'inin kolonoskopi için ana endikasyonu intestinal Behçet Hastalığı idi.* ***Bulgular:*** *Toplam 135 intestinal Behçet hastasında ileokolonik tutulum olup olmadığını anlamak için kolonoskopi yapıldı. 135 hastanın 8'inde (%5,9) ileal ve kolonik ülserler saptandı. İatrojenik perforasyon üç olguda (%2,22) görülürken, bunların 2'sinde proksimal kolon ve ileum'da ülserler bulundu. Üçüncü olgunun ülserleri sigmoid kolon, inen ve transvers kolon segmentlerindeydi. Bu 3 olgunun hepsi de ileal rezekziyon ve sağ hemikolektomi için cerrahiye gönderildiler.* ***Sonuç:*** *Behçet Hastalığında yalnız tanı için değil, aynı zamanda Behçet Hastalığının intestinal tutulumunun sürveyansı için kolonoskopi muayenesi çok yaygın olarak kullanılır. Volkan biçimli ülserler perforasyona özellikle eğilimlidirler. Konoskopi sırasında aşırı hava verilmesi perforasyona sebep olabileceğinden klinisyenler ve endoskopistler bu konuda uyanık olmalıdır. Ayrıca hastalar; kolonoskopik inceleme sonrasında karın ağrısı durumunda mutlaka takip edilmeli ve kolonik perforasyon her zaman akılda tutulmalıdır.*

Anahtar kelimeler: *Behçet hastalığı, kolonoskopi, ileokolonik perforasyon*

INTRODUCTION

Behcet' s disease (BD), is a multisystem inflammatory disorder characterized by repetitious oral and genital ulcers, skin lesions and relapsing ocular lesions that may affect the nervous system, joints, blood vessels and sometimes the gastrointestinal system (1,3). Gastrointestinal involvement rates vary widely, estimated at 3 to 60 per cent in different countries (4-11).

Intestinal BD lesions can range from simple mucosal inflammation, to infarct or ischemia due to small or large vessel involvement. These findings may vary from non-specific colitis to diffuse ulcers (12). Lesions arise mostly from the ileocaecal segment with colonic involvement seen less frequently (13).

Intestinal BD is an important morbidity and mortality reason depending on serious complications it causes (14,15). Massive hemorrhage, fistulisation and intestinal perforation are complications encountered in approximately 50% of patients suffering from intestinal BD (14,16,17). Free perforation is a state with a poor prognosis that may increase the risk of panperitonitis, a complication that requires emergent operation (14,18,19). However, there is no data about iatrogenic perforation during the colonoscopy in intestinal BD patients. In the current study, data from BD patients who experienced perforation during or after a colonoscopy procedure were retrospectively analyzed.

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Correspondence: Mehmet BEKTAŞ
Ankara University School of Medicine,
Department of Gastroenterology, Ibn-i Sina Hospital, Sihhiye-Ankara
Phone: +90 312 508 21 50 • **E-mail:** mbektas@medicine.ankara.edu.tr
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MATERIALS and METHODS

One hundred thirty five BD patients underwent colonoscopy to evaluate lower gastrointestinal system involvement between May 2002 and December 2007. All patients met the diagnostic criteria defined by the International Study Group for Behcet's Disease (23). Patients who met at least two or more active clinical symptoms related to BD were categorized as in the active BD group, whereas subjects who had no symptoms other than repetitious oral ulcers at least until a month ago were classified as in the inactive BD group (23,24).

Preparation for colonoscopy in all patients was done using Fleet phospho-soda 90 mL (C.B. Fleet Co., Inc. Lynchburg, VA, USA). Midazolam, meperidine and propofol were used as pre-procedural sedatives. All colonoscopies were done by an experienced endoscopist (M.B.) using an advanced imaging technique videocolonoscopy (Fujinon E400 Tokyo, Japan). A total of 2480 colonoscopies were done in the same time period due to other indications. In the study, we retrospectively analyzed BD patients who suffered from perforation during or after colonoscopy.

RESULTS

Of the 135 BD patients (77 female, 58 male), in our study, mean age 35.4 (range, 18-69). Eight (5.9%) patients of the 135 had ileal and colonic ulcers and the rest (127 cases) had normal colonoscopy examinations. These patients had hematochezia, abdominal pain as a gastrointestinal symptom and anemia as laboratory findings. Some of the ulcers were reported to be superficial aphthous lesions whereas others were defined as profound ulcers. Three of the 8 patients (2.2%), had ileal and colonic ulcers; and five (3.7%) had colonic involvement alone. Biopsies were taken from all ileal and colonic lesions for histopathological examination and the results revealed vasculitis. The characteristics of the patients are summarized in Table 1. Iatrogenic colon perforation during colonoscopy was encountered in 3 male patients, mean age 33.6 years (range, 18-56).

A total of 2480 colonoscopies were performed in the same time period due to other indications such as constipation, abdominal pain, diarrhea, inflammatory bowel disease, weight loss, rectal bleeding and iron deficiency anemia. 240 (9.17%) patients of 2480 were diagnosed with Crohn's Disease; 276 (10.5%) had ulcerative colitis; and 46 (1.75%) had colorectal cancer;no subjects among these groups suffered colonoscopic perforation as a complication.

The terminal ileum was reached in all of the BD patients, except the three who experienced iatrogenic perforation; two of the three patients were examined until the ceacum; profound ulcers were seen in the proximal colon (Figure 1). The third patient's was examined up until mid-transverse colon where profound ulcers were observed in the sigmoid, descending and transverse colon. Abdominal distention, pain, desaturation, hypotension and tachycardia developed during the procedure in all three patients. Physical examination revealed defense and rebound findings. The abdominal X- ray results were free of intraperitoneal air. Emergency surgery was performed on all three patients. Two of the perforations were seen in ileum and one in ascending colon during intraoperative examination. Ileal resection and hemicolectomy were performed on all three patients (Figure 2) and histopathological examination from these patients' resection materials revealed vasculitis (Figure 3).

DISCUSSION

Intestinal involvement in BD is seen in 1 to 60% of patients (14,16,17). Intestinal BD may be diagnosed in a patient if s/he meets criteria for BD by systemic findings and typical ulcers are seen either in small intestine or colon (15-17). Documentation of typical ulcerative lesions using objective modalities is performed in only 3- 25% of BD cases (12,14). In this

Table 1. Demographics of the patients who had ulcers as a finding of colonoscopic evaluation

No	Age	Sex	OU	GU	A	PT	U	PPE	EN	Symptom	Colonoscopy	Perforation
1	18	M	+	+	+	+	-	-	+	Hematochesia	Colonic ulcer	Ileum
2	26	M	+	+	-	+	+	+	-	Hematochesia	Ileal-colonic ulcer	Ileum
3	56	M	+	+	-	-	+	+	+	Hematochesia	Colonic ulcer	Ascending colon
4	53	F	+	+	-	+	-	+	-	Hematochesia	Colonic ulcer	None
5	25	F	+	+	+	+	-	+	-	Anemia	Ileal-colonic ulcer	None
6	52	F	+	+	-	+	+	+	-	Hematochesia	Colonic ulcer	None
7	69	M	+	+	-	+	+	+	+	Anemia	Colonic ulcer	None
8	34	M	+	+	+	+	-	+	-	Anemia	Ileal-colonic ulcer	None

OU = Oral ulceration; GU = Genital ulceration; A = Arthritis; PT = Pathergy test; U = Uveitis; PPE = Papulopustular eruptions; EN = Erythema nodosum;

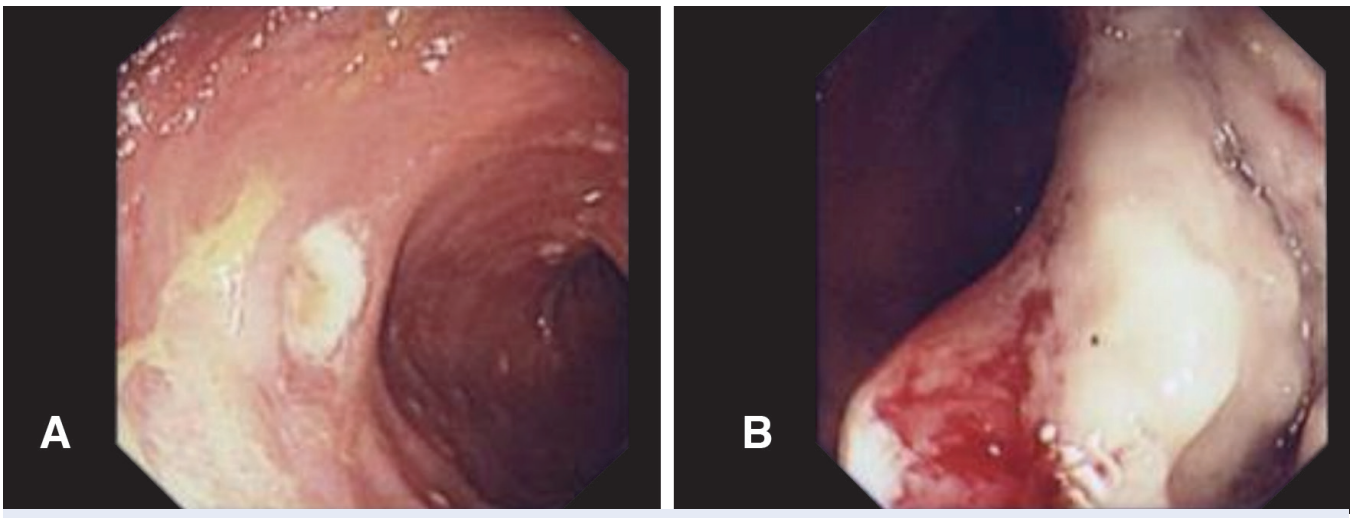

Figure 1. A. Proximal colonic ulcer, **B.** Ileal deep ulcer.

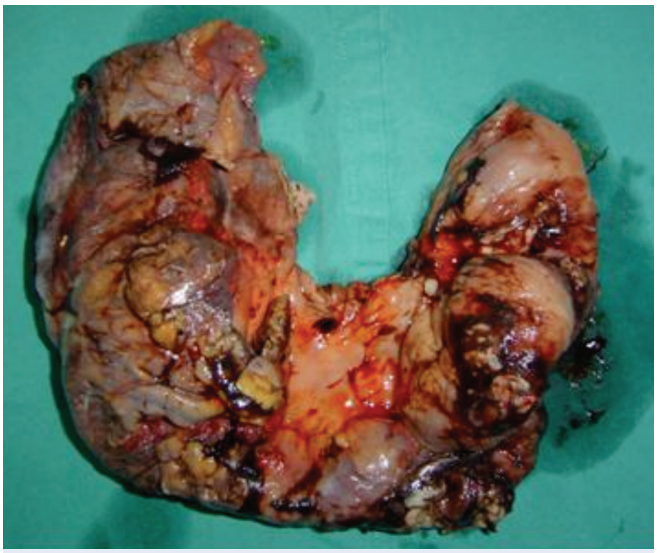

Figure 2. Right hemicolectomy material.

study, 8 (5.9%) out of 135 patients were determined to have ileocolonic involvement; 4 (2.9%) had superficial aphthous ulcers; and the other 4 (2.9%) had volcano-shaped profound ulcers. In a study of 50 BD patients by Köklü et al., only 2% of patients had endoscopic colitis but the rate increased to 15% upon histopathological examination in these patients (19,20).

Intestinal BD can cause serious complications - massive hemorrhage, fistulisation and intestinal perforation are complications encountered in approximately 50% of patients. Free perforation can lead to panperitonitis, requiring an emergent operation with a poor prognosis (14,18,19). The studies reveal that free intestinal perforation is more frequently seen in Far Eastern countries (27). The pathophysiology of perforation in intestinal BD is unclear; nevertheless, we have put forth the following considerations: (1) Typical intestinal BD ulcers are usually large, separate and excavated in shape (28,30,31). (2) Combined intestinal dilatation may contribute to perforation. High intraluminal pressured intestinal distention, proximal to the obstructed segment, may increase perforation risk (32-34), (3) Long term steroid use may be related to intestinal perforation development;steroid treatment may cause peritonitis by inhibiting the closing process of perforation (35).

Risk factors for intestinal perforation, defined in the literature, are - a younger age at the time of diagnosis, and a history of operation and volcano shaped intestinal ulcers (36-39). Kim et al. Found volcano shaped ulcers had a greater risk of spontaneous intestinal perforation than other types of ulcers (33). In our study, all patients with intestinal perforation had either volcano shaped or profound ulcers. There was no history of steroid use these patients. The age of patients who suffered perforation was between 18 and 56. Three of the patients were evaluated due to hematochezia, and 2 of the

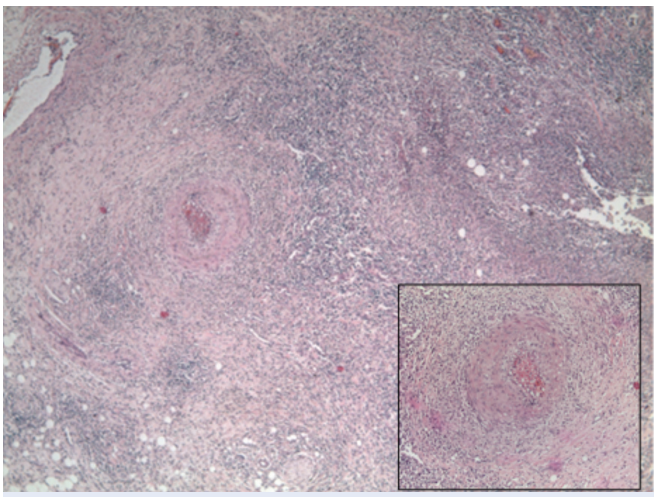

Figure 3. Severe inflammation and vasculitis in the ileum wall (H&E,x40, inset: H&E,x100).

colonoscopies revealed volcano shaped ulcers in both ileum and proximal colon; the third case exhibited profound ulcers in the sigmoid, descending and transverse colon. In another study by Moon et. al, 33 patients (25.6%) of 129 symptomatic intestinal Behcet's patients were diagnosed with intestinal perforation; it was emphasized that all cases were operated and the age of patients ranged from 12 to 70, with a mean age of 33.8 years (38). In our study, there was no history of acute abdominal pain or free perforation from colon and ileum. All perforations occurred after the colonoscopy procedure. Our experience is the first documentation highlighting the high risk of ileocolonic perforation during colonoscopies in intestinal BD patients.

Ileal segmental resection and right hemicolectomy are the preferred method to treat spontaneous perforation in order to decrease both perforated intestinal BD incidence and relapse rates (18,19). In a study of 7 cases by Sayek et al. right hemicolectomy and ileal resection were performed in 6 patients while the 7th patient underwent right hemicolectomy alone, secondary to intestinal anastomosis leakage (18). Many other studies, composed of small surgical series, have evaluated results of perforation patients after the incident to determine the rate of relapse after operation and found that a history positive for intestinal perforation and fistulisation increased the risk for re-perforation and that the suggested length of resection was controversial (40). Kim et al., determined that relapse rates were 13% (3 out of 23 patients), and 50% (8 out of 16), in medical treatment and operation groups respectively (33). Our patients underwent ileal resection and right hemicolectomy, following a similar surgical fashion; no secondary surgical procedure was necessary. All resection materials from the three perforated patients showed vasculitis upon histopathological examination.

It is also important to attain full remission in perforated cases during the early post-operative period to prevent relapses. As in inflammatory bowel diseases, sulphasalazine and steroids are the preferred first line treatment choices (45,46). Most systemic or local medications are either given alone, or combined with colchicine and steroids (45-47). In our series, we were able to achieve remission with colchicine, corticosteroid and azathioprine therapy, and there have been no exacerbations experienced during our 3-year follow up period.

Endoscopic procedures such as gastroscopy and colonoscopy are widely used for the diagnosis of gastrointestinal system diseases. Colonic perforation resulting from colonoscopic and sigmoidoscopic procedures is a rare but serious complication with high rates of morbidity and mortality (48-51). The frequency of perforations after colonoscopy is estimated to be 0.03% to 0.8% for diagnostic colonoscopy and 0.15% to 3% for therapeutic colonoscopy (22). Perforations that occurs during diagnostic colonoscopy are due to direct mechanical penetration with the instrument tip, sharp flexion of the colonoscope, high pressure applied when a loop is formed or barotrauma as a result of aggressive gas insufflations (23,24). In a retrospective study, the most common underlying cause for bowel perforation was direct mechanical injury of the colonic wall by the colonoscope. It occurred in patients with diverticular disease or a strictured, severely diseased colonic segment. These risk factors were in accordance with those noted in the literature (52,53). The most frequent site of perforation was the sigmoid colon, similar to other studies (54-57). which may be explained by its anatomical characteristics of frequent redundancy, or narrowing from diverticular disease, or adhesions after previous pelvic operations (57).

In this study, iatrogenic colon perforation did not occur in Crohn's disease or ulcerative colitis patients. There were no histories of abdominopelvic operation in BD patients and colonic diverticula were not seen during the colonoscopic examination in this group. We thought that barotrauma induced perforation for all perforations occurred in the proximal colon.

In conclusion, colonoscopy is a scanning modality that is not only diagnostic but may also be used periodically during follow- ups, or to display relapses responsive to medical treatment. Perforation may develop during colonoscopy a procedure, especially discrete ulcers that typically have a round or oval "punched-out" appearance with a tendency to bleed or perforate. For these reasons, during the colonoscopy procedure, a low pressure of air should be applied for minimal barotrauma and maximum caution for perforation should be shown during after the procedure and is subsequent follow up appointments.

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