Original Article

Relationship between backwash ileitis and macroscopic findings of resected large bowel in patients with ulcerative colitis

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Abstract

Background. Backwash ileitis（BWI）is defined as ulcerative colitis（UC）-like inflammation extending beyond the ileocecal valve. This inflammation is homogeneously and diffusely distributed over the ileum. BWI has been suggested as a risk factor for colon cancer and pouchitis. Preoperative diagnosis of BWI is generally difficult. This study aimed to clarify the characteristics of UC patients with BWI and the clinical significance of BWI.

Methods. Patients who had undergone any kind of bowel resection for UC at Saitama Medical Center, Jichi Medical University, between September 1993 and September 2010 were included in this study. The relationship between BWI and various clinical factors, including, patient characteristics, preoperative endoscopic findings, postoperative histological findings, and postoperative course, was investigated.

Results. Of the total of 53 patients, 3（5.7%）presented with BWI. BWI was significantly correlated with the presence of extensive or longitudinal large bowel ulcers.

Conclusions. BWI may be a complication in UC patients diagnosed with extensive or longitudinal ulcers in the large bowel before surgery. In such cases, careful intraoperative observation of the resected ileum is imperative.

（**Keywords**：Ulcerative colitis, Backwash ileitis, Longitudinal ulcer）

Introduction

Ulcerative colitis（UC）is an inflammatory disease involving the large bowel. It is generally diagnosed on the basis of clinical symptoms and colonoscopic findings. Typical clinical symptoms of UC include diarrhea, visible blood in the stool, abdominal pain, fever, and weight loss[1]. Characteristic endoscopic findings of UC include various levels of continuous bowel inflammation extending from the rectum, such as mucosal erosion, ulcer, and pseudopolyposis[2]. Longitudinal ulcers are generally observed in Crohn's disease（CD）but they are also present in a few patients with UC, making differentiation of UC from CD difficult[3].

In UC patients, inflammatory changes in the small bowel are occasionally encountered. Such abnormalities raise the possibility of CD and cause hesitation in reaching a definite diagnosis of UC. Inflammation of the terminal ileum in UC patients is called backwash ileitis（BWI）, which is defined as ulcerative colitis（UC）-like inflammation extending beyond the ileocecal valve. The inflammation is homogeneously and diffusely distributed over the ileum[4, 5]. Although BWI has been reported in some studies as a risk factor for postoperative colon cancer or pouchitis, which is characterized by symptoms of pouch dysfunction associated with endoscopic and histological evidence of nonspecific acute inflammation of the pouch mucosa[6], its clinical significance remains unclear[6-9]. This study clarified the characteristics of UC patients with BWI and the clinical significance of BWI.

Methods

Patients who had undergone any kind of bowel resection for UC（including resection of the terminal ileum）at Saitama Medical Center, Jichi Medical University between September 1993 and September 2010 were included in this study. By retrospective review of medical records, we investigated the relationship between BWI and various clinical factors, including patient characteristics, preoperative endoscopic

findings, histological and macroscopic findings of the resected specimens, and postoperative course. The clinical severity of colitis was classified as mild, moderate, or severe on the basis of the Japanese clinical guidelines for UC treatment[1]. Factors determining disease severity included stool frequency, visible blood in the stool, fever, tachycardia, anemia, and erythrocyte sedimentation rate. The endoscopic severity of colitis was classified as grade 1 to grade 4 using Matts' grade, which determines the most severe inflammatory findings in the area observed endoscopically[10]. In this study, Matts' grade 4, which indicates severe ulceration of the mucosa with hemorrhage, was defined as the most severe type of colitis.

Distribution and severity of inflammation and the presence of BWI were confirmed by examination of the macroscopic features of the resected specimens. The presence of dysplasia and cancer was determined via a retrospective review of the histopathology reports. A diagnosis of BWI was made if an inflammatory ulcer or erosion was found in the terminal ileum[5]. The occurrence of postoperative pouchitis was confirmed from retrospective review of the medical records, including postoperative endoscopic reports. A diagnosis of pouchitis was made if the ulcer or erosion was found in the ileal pouch[13].

Fisher's exact test was used to compare categorical and binary data. Student's t-test was used to analyze continuous data. The level of statistical significance was set at $P < 0.05$.

Results

In total, 55 consecutive patients were analyzed in this study. Two patients, one diagnosed with CD after surgery and one without a postoperative histopathological report, were excluded from the study. The postoperative diagnosis of CD was made on the basis of an intraoperative finding of ileal stenosis, which is not commonly observed in UC patients, although the histological findings for this patient could not completely rule out the possibility of UC. Therefore, the study group comprised 23 females and 30 males aged 16-71 years. Twelve patients had clinically severe UC, 48 had pancolitis, and 44 had undergone pouch operations (Table 1). BWI was present in tree patients (5.7%) as determined from the resected specimens. Of the three patients, a well demarcated ileal ulcer (7cm) was revealed in one, whereas erosions rather than well-demarcated ulcers were found in the terminal ileum in the other two patients. BWI was not diagnosed before surgery in these three patients, and histological findings for the resected specimens were not suggestive of CD. BWI was significant correlated the presense of extensive or longitudinal large bowel ulcers in the large bowel of the resected specimens (Table 2, Figure 1). Tree patients were followed up for less than 6 months; therefore, they were excluded from the analysis. During the postoperative observation period, which ranged of 6-84 months, 15 (36.6%) of 41 patients in whom pouch surgery was performed were diagnosed with pouchitis by annual or biannual surveillance colonoscopy. No significant factor was associated with the occurrence of postoperative pouchitis (Table 3).

Table 1. Patient characteristics（n=53）

Mean age（yr）at operation	40.2
Gender-Females	23
Clinical severity of colitis	
Mild	4
Moderate	37
Severe	12
Extent of colitis	
Left-sided	5
Pancolitis	48
Bowel status at analysis	
Ileal J pouch	44
Ileorectal anastomosis	3
Ileostomy	6

Table 2. Characteristics of patients with ulcerative colitis with or without backwash ileitis

Variables	Backwash Ileitis（-）(n=50)	Backwash Ileitis（+）(n=3)	P Value
Mean age（yr）at operation	41.3	22.7	0.582*
（SD）	57.4	29.3	
Gender-Females	21	2	0.754
Pancolitis	45	3	0.659
Clinically Severe Type	10	2	0.68
Endoscopically Severe Type（Matts grade 4）	21	3	0.173
Postoperative macroscopic findings of ulcer-affected area			
All over	5	3	<0.001
More than half-proportion	16	3	0.077
Involving longitudinal ulcer	10	3	0.015
Comorbid Cancer or Dysplasia	9	0	0.662

P-value represents the result of Fisher's exact test unless otherwise spwcified.
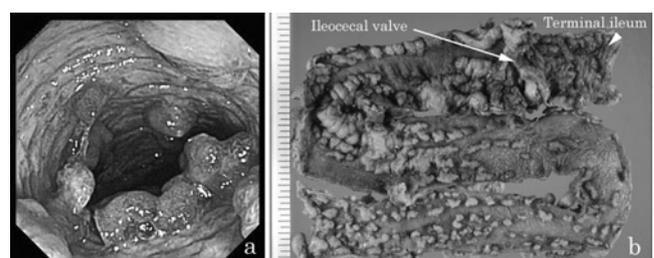*Student's t-test

Figure 1. Case study of a 26-year-old female patient with ulcerative colitis and backwash ileitis
Preoperative colonoscopy showed deep and circumferential ulcers in the sigmoid colon（a）. Extensive ulceration was observed throughout the resected colon specimen. Ulcers

ranged from the rectum to the terminal ileum and were longitudinal in shape（b）.

Table 3. Comparision of clinical factors between patients with and without postoperative pouchitis

Variables	Pouchitis (-) (n=26)	Pouchitis (+) (n=15)	P Value
Mean age（yr）at operation	40.5	39.6	0.874*
（SD）	16.7	15.9	
Gender-Females	13	5	0.478
Endoscopically Severe Type（Matts grade 4）	10	7	0.854
Postoperative macroscopic findings of ulcer-affected area			
All over	4	2	0.78
More than half	9	4	0.853
Backwash ileitis	0	1	0.778

P-value represents the result of Fisher's exact test unless otherwise spwcified.
*Student's *t*-test

Discussion

BWI was first reported by McCready et al. in 1949[4]. It is defined as UC-like inflammation extending beyond the ileocecal valve. The inflammation spreads homogeneously and diffusely over the ileum[5]. The reported incidence of BWI ranges from 10% to 35%[11, 12]. The incidence reported in the present study was lower than that previously reported（5.7%）. Many investigators have reported the clinical significance of BWI. Some studies reported that BWI can be a risk factor for pouchitis, which is a serious postoperative complication occurring in 36%-60% patients who undergo pouch operations for UC[6, 13-15]；however, the result of other studies did not support this finding[7, 8, 16]. No significant correlation between pouchitis and BWI was observed in our study. Heuschen et al. reported that BWI is a risk factor for colon cancer[9], but the results of the present study showed no such relationship. However, our analysis was performed with data for a limited number of patients. A larger sample may yield different results.

The current study demonstrated a significant correlation between BWI and extensive or longitudinal ulcers in the large bowel. Although Igarashi et al. reported pancolitis in all of 13 BWI patients analyzed in their study[5], the relationship between the extent of large bowel ulceration and BWI was unclear. Therefore, severe inflammatory changes in the large bowel may be among the most important factors associated with BWI occurrence. Nevertheless, the present study identified no significant relationship between BWI and the clinical or endoscopic severity of UC. These inconsistent results may be attributed to differences in the diagnostic approach toward the severity of UC. In fact, endoscopic severity is determined by the most severe finding in the observed area, with no reference to the extent of inflammation. The results derived from this process can differ from those determined by macroscopic findings, which reflect the overall features of the resected large bowel. All UC patients with BWI in our study sample were endoscopically classified as severe cases.

This study demonstrated that many ulcers in UC patients can be longitudinal. A 17% incidence of longitudinal ulcers in UC patients has been reported in the past; such ulcers are usually seen in patients with serious disease requiring surgery[2, 3]. Longitudinal ulcers are generally seen in CD patients, and ileitis is also a common characteristic of CD. The results of this study indicate a strong correlation between BWI and presence of longitudinal ulcers. Therefore, sufficient care should be taken during the process of arriving at a definite diagnosis of BWI in UC-like patients with ileitis[2, 3, 17].

Although BWI is universally believed to be a reaction to the reflux of colonic contents into the terminal ileum[4, 12], Abdelrazeq et al. reported that the presence of ileitis in UC patients indicates primary involvement of the terminal ileum, which is due to the same process of mucosal inflammation observed in the large bowel[15]. Recently, the term "indeterminate colitis" has been applied to biopsy specimens wherein differentiation between UC and CD is not possible[18, 19]. A report by Guindi and Riddell suggested that UC with BWI should be diagnosed as "inflammatory bowel disease, CD not excluded"[19]. Our findings indicate that UC must be carefully differentiated from CD in patients with BWI that is ileal in origin and not a form of back wash ileitis caused by UC.

Some reports recommend that an inflamed terminal ileum should be resected at the time of surgery for UC[4, 5]. However, preoperative diagnosis of BWI can be difficult because total colonoscopy involving the terminal ileum is not frequently performed in order to avoid stress to the large bowel in severe UC cases[20]. BWI should be strongly suspected if extensive involvement of the large bowel with ulceration or longitudinal ulcers is identified during preoperative examination. When preoperative colonoscopic observation is limited to the distal large bowel, which is often the case in patients with severe inflammation, instant enema or air enema can be useful tools to determine the extent of ulceration in the large bowel. If BWI is suspected before surgery, the resected ileum must be observed more carefully during surgery. If an ulcer is detected in the cut line of the ileum, additional resection must be performed.

In conclusion, this study demonstrated a significant connection between the presence of extensive or longitudinal large bowel ulcers and BWI. In addition, preoperative prediction of BWI may be possible. We recommend more careful intraoperative observation of the resected ileum and adequate resection of the ileum in UC patients with these preoperative findings.

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潰瘍性大腸炎における Backwash ileitis と大腸切除標本肉眼所見の関係

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要　　約

背景
Backwach leitis（以下，BWI）は，潰瘍性大腸炎において炎症が回盲弁をこえて回腸へ及んだ病態である。BWI は大腸癌や回腸嚢炎の危険因子とされている。また，BWI を術前診断することはしばし困難とされる。BWI を伴った潰瘍性大腸炎の特徴とその臨床的意義について調べた。

方法
対象は，1993年 9 月から2010年 9 月までの間に，自治医大さいたま医療センターで腸切除術を施行された，潰瘍性大腸炎の症例である。臨床所見，術前内視鏡所見，術後病理所見，術後経過と，BWI の関係を調査した。

結果
対象53例のうち， 3 例（5.7％）に BWI を認めた。大腸潰瘍の範囲と BWI の間，縦走潰瘍と BWI の間に，有意な関連を認めた。

考察
結腸に広範囲または縦走する潰瘍を認める症例は BWI を伴う可能性が高い。術前にこれらの所見を認める場合は，術中に切除回腸を十分に確認する必要がある。

（キーワード：潰瘍性大腸炎，Backwach leitis，縦走潰瘍）