Rectal-sparing type of ulcerative colitis predicts lack of response to pharmacotherapies

Yuki Horio 1*, Motoi Uchino 1, Toshihiro Bando 1, Teruhiro Chohno 1, Hirofumi Sasaki 1, Akihiro Hirata 1, Yoshio Takesue 2 and Hiroki Ikeuchi 1

Abstract

Background: Ulcerative colitis (UC) is known as an immune disorder of the colon that generally involves the rectum, but an atypical distribution of inflamed mucosa has previously been noted in certain subtypes of UC, such as the rectal-sparing type (RST). As noted in a previous report, patients with the RST may be at elevated risk for disease refractoriness, but the clinical significance of RST remains unknown.

Methods: UC patients who underwent surgery between January 2010 and April 2015 were included. Patients were classified as having the RST or a non-RST based on colectomy specimens or a pre-operative endoscopy. Possible risk factors for urgent/emergent surgery were analyzed. We specifically determined whether the RST is a significant predictor for urgent/emergent surgery.

Results: In total, 46/482 patients were classified as having the RST. Disease severity was significantly worse in patients with the RST than in other patients (p = 0.02). Urgent/emergent surgery was required for 24/46 patients with the RST, compared with 107/436 non-RST patients (p < 0.01). The overall incidence of urgent/emergent surgery was 131/482. Disease duration < 70.2 months [odds ratio (OR) 2.45], severe disease (OR 87.1), total administered steroid dose < 5000 mg (OR 3.02), daily pre-operative steroid dose ≥ 9 mg (OR 2.59), and the RST (OR 5.59) were identified as independent risk factors for urgent/emergent surgery.

Conclusion: The RST was an independent risk factor for urgent/emergent surgery in our analysis of surgically treated patients with UC.

Keywords: Ulcerative colitis, Rectal-sparing, Urgent/emergent surgery, Inflammatory bowel disease
in pediatric patients [11–14]. Although RST patients exhibited a high risk for refractory disease in a previous report [15], the clinical significance of the RST remains unknown.

We recently treated several UC patients with the RST who required urgent/emergent surgery. Therefore, we retrospectively reviewed clinical records to evaluate clinical features of RST patients and the association between the RST and failure of medical therapy (i.e., need for colectomy).

Methods

Patients

UC patients who underwent a laparotomy at Hyogo College of Medicine between January 2010 and April 2015 were included in this study. All colectomy specimens with histologic features of UC and no Crohn’s-like features such as granulomas, transmural lymphoid aggregates, or fissures were identified. Gender, age at onset of UC, age at initial surgery, duration of disease, disease severity, total administered prednisolone (PSL) dose, daily pre-operative PSL dose, immunomodulator administration, biologic administration, and timing of surgery, including whether surgery was urgent/emergent or elective, were retrospectively determined using clinical records. UC disease activity was assessed primarily according to clinical features using the criteria of Truelove and Witts [16]. Total administered corticosteroids were converted into the PSL dose and calculated based on the administered corticosteroid dose since the initial onset of UC. The types of immunomodulators, including calcineurin inhibitors and thiopurines, and biologics administered were determined based on medication history, irrespective of the dosing period.

Definition of the RST of UC

Patients were classified as having the RST or a non-RST (i.e., ordinary diffuse proctocolitis). The RST was noted when the rectum was obviously spared of active or chronic inflammation, and relatively little or no inflammation was observed at the rectum compared to proximal colitis in colectomy specimens. Alternatively, the RST was noted when rectal inflammation was limited to a Mayo endoscopic score of 0 or 1 and was also milder than that of the proximal colon based on pre-operative endoscopy. All endoscopic findings were assessed by expert physicians at our institution who were familiar with UC, age at initial surgery, duration of disease, disease severity, existence of the RST, total administered PSL dose, daily pre-operative PSL dose, and immunomodulator or biologic administration, were analyzed to identify significant predictors. Tacrolimus (TAC) or cyclosporine (CsA) is administered as rescue therapy for severe steroid-refractory UC, and azathioprine (AZA) or mercaptopurine (6-MP) is used to maintain remission. Therefore, we analyzed immunomodulator administration based on two categories: TAC/CsA and AZA/6-MP.

Primary outcome

The primary end point was urgent/emergent surgery. Possible risk factors for urgent/emergent surgery, including gender, age at onset of UC, age at initial surgery, duration of disease, disease severity, existence of the RST, total administered PSL dose, daily pre-operative PSL dose, and immunomodulator or biologic administration, were analyzed to identify significant predictors. Tacrolimus (TAC) or cyclosporine (CsA) is administered as rescue therapy for severe steroid-refractory UC, and azathioprine (AZA) or 6-mercaptopurine (6-MP) is used to maintain remission. Therefore, we analyzed immunomodulator administration based on two categories: TAC/CsA and AZA/6-MP.

Surgical indications and timing of surgery

At our institution, the absolute indications for emergent surgery include massive hemorrhage and free perforation. Indications for urgent surgery performed within 24 h of admission include severe or fulminant colitis with or without toxic megacolon that is unresponsive to conventional maximal pharmacotherapies and less severe colitis with medically intractable or intolerable pharmacotherapy side effects with a progressively worsening general condition. Elective surgery was indicated for refractory disease or extra-intestinal manifestations without a progressively worsening general condition or complicated carcinoma or dysplasia. The standard surgical procedures for UC at our institution include total proctocolectomy and ileal pouch anal anastomosis (IPAA) with or without an ileostomy. A total colectomy with mucous fistula and end ileostomy was mainly performed as an emergency surgery. This procedure was performed for patients with free perforation, toxic megacolon, or fulminant colitis with progressive worsening to severe sepsis or septic shock.

Exclusion criteria

We excluded patients from the RST group who were treated with topical treatments.

All colectomy specimens were identified as UC based on histological features. Patients with a diagnosis or suspicion of Crohn’s disease based on histological findings were not included in this series.

Statistical analysis

The statistical analysis was performed as follows. Categorical variables were compared using a chi-squared test. Numerical variables are expressed as medians and ranges and were compared using the Mann-Whitney U test. The cut-off values for age at onset of UC, age at initial surgery, duration of disease, total administered PSL dose, and pre-operative PSL dose were defined as the median values in this series (32 years, 44 years, 70.2 months, 5000 mg, and 9 mg, respectively). The level of statistical significance was set at $p < 0.05$. The odds ratio (OR) and 95% confidence intervals (CIs) were calculated for all variables in the univariate analysis. Each individual factor with a significant $p$-value in the
univariate analyses was subsequently entered into a stepwise logistic regression model. JMP ver.12 (SAS Institute Inc., Cary, North Carolina, USA) was used to perform all analyses.

**Ethical statement**

All study protocols were approved by the institutional review board of Hyogo College of Medicine (no. 2078). Informed consent and approval for the use of patient data were obtained prior to surgery.

**Results**

**RST characteristics**

A total of 482 patients who underwent a colectomy were analyzed. The clinical characteristics of patients are presented in Table 1. Overall, 46/482 (9.5%) patients had the RST of UC. Figure 1 presents a typical RST colectomy specimen. No significant differences in gender, age at onset of UC, and age at initial surgery were noted between the RST and non-RST groups. The time from onset of UC to initial surgery was significantly shorter for patients with the RST than for patients with a non-RST ($p < 0.01$). The disease severity was classified as severe in 18 patients (39.1%) and fulminant 3 (6.5%) patients with the RST, resulting in a significantly higher rate of severe disease in RST patients ($p = 0.02$).

Regarding pharmacotherapy, patients with the RST were significantly more likely to have received immunomodulators ($p = 0.04$), but the other therapies were not significantly different between the groups. The surgical indication was cancer in 1 (2.1%) patient and dysplasia in 1 (2.1%) patient with the RST. In contrast, among subjects with a non-RST, the surgical indication was cancer in 64 (14.7%) patients and dysplasia in 44 (10.1%) patients. In addition, urgent/emergent surgery was required for 24/46 (52.2%) patients with the RST and 107/436 (24.5%) patients with a non-RST; the rate of urgent/emergent surgery was significantly higher among patients with the RST ($p < 0.01$).

**Primary outcome**

The overall incidence of urgent/emergent surgery was 131/482 (27.2%). Univariate and multivariate analyses were performed to identify independent risk factors for urgent/emergent surgery. The results of univariate analyses of risk factors potentially associated with urgent/emergent surgery are presented in Table 2. Age at initial surgery < 44 years, duration of disease < 70.2 months, severe/fulminant disease, total administered PSL dose < 5000 mg, daily pre-operative PSL dose $\geq 9$ mg/day, and the RST were significant risk factors for urgent/emergent surgery. Patients who underwent elective surgery were significantly more likely to have received AZA/6-MP ($p < 0.01$). TAC/CsA administration was not significantly different between the groups. In addition, the seven statistically significant factors mentioned above were entered into the multivariate logistic regression analysis (Table 3). Duration of disease < 70.2 months (OR = 2.45, 95% CI 1.10-5.54, $p = 0.03$), severe/fulminant disease (OR = 87.1, 95% CI 40.9-205.1, $p < 0.01$),

### Table 1 Patients characteristics

|                       | All patients $n = 482$ | RST $n = 46$ | non RST $n = 436$ | $p$- value |
|-----------------------|------------------------|--------------|------------------|-----------|
| Gender (Male/Female)  | 316/166                | 29/17        | 287/149          | 0.74      |
| Age at onset of UC (years) | 35.7 ± 17.4          | 35.7 ± 18.8  | 35.7 ± 17.3      | 0.99      |
| Age at initial surgery (years) | 44.6 ± 16.7          | 41.2 ± 19.3  | 44.9 ± 16.4      | 0.15      |
| Disease duration (months) | 70.2 (0.2-479.7)      | 31.4 (1.1-347.3) | 73.6 (0.2-479.7) | $<0.01^*$ |
| Severe/Fulminant disease | 145 (30.1)           | 21 (45.7)    | 124 (28.4)       | 0.02      |
| Total given PSL dose (mg) | 5000 (0-200,000)     | 4535 (300-47,000) | 5000 (0-200,000) | 0.76      |
| Daily pre-operative PSL dose (mg/day) | 9(0-80)             | 12.5(0-80)   | 7.5(0-80)        | 0.38      |
| Immunomodulators administration | 247 (51.2)        | 30 (65.2)    | 217 (49.8)       | 0.04      |
| Biologics administration | 127 (26.3)         | 11 (23.9)    | 116 (26.6)       | 0.69      |
| Surgical indication cancer/dysplasia | 110 (22.8)       | 2 (4.3)      | 108 (24.8)       | $<0.01^*$ |
| free perforation | 27 (5.6)             | 2 (4.3)      | 25 (5.7)         |           |
| refractory disease | 343 (71.2)           | 42 (91.3)    | 301 (69.0)       |           |
| EIMs | 2 (0.4)             | 0            | 2 (0.4)          |           |
| Urgent/emergent surgery | 131 (27.2)          | 24 (52.2)    | 107 (24.5)       | $<0.01^*$ |

RST = rectal sparing type, UC = ulcerative colitis, PSL = prednisolone, EIMs = extra intestinal manifestations

Data are numbers with percentages in parentheses unless otherwise indicated

Continuous variables are indicated as mean ± standard deviation and median (range)

$^* p < 0.05$ (Significantly different)
total administered PSL dose < 5000 mg (OR = 3.02, 95% CI 1.39-6.76, \( p < 0.01 \)), daily pre-operative PSL dose \( \geq 9 \) mg (OR = 2.59, 95% CI 1.20-5.65, \( p = 0.02 \)), and the RST (OR 5.59, 95% CI 1.90-16.9, \( p < 0.01 \)) were identified as independent risk factors for urgent/emergent surgery.

**Discussion**

The RST of UC may occur at some point during the medical treatment of UC in as many as 44% of cases [17]. This result may indicate that only the timing of the disease or the extent of disease may be revealed by treatment modifications. According to a previous report, the RST exclusively exhibits one course of disease progression because histological inflammation was consistently defined. These results suggest that an absolute RST does not exist, and most RST cases consist of a relative RST [18, 19]. In addition, Park et al. [18], reported that most RST patients develop remarkable, visible inflammation during disease progression. Therefore, we first excluded patients who received topical treatments from the RST group. Unfortunately, the initial degree of rectal inflammation, alteration and progression of the disease, and timing of RST appearance before surgery could not be evaluated retrospectively. However, RST diagnosed immediately before surgery was an independent risk factor for urgent/emergent surgery in this series. Urgent/emergent surgery may indicate refractoriness and resistance to pharmacotherapies. Oshitani et al. [15] reported that patients with endoscopically defined RST exhibited enhanced refractoriness and increased recurrence rates and had a longer duration of active disease than patients without the RST. Therefore, presence of the RST may predict a future colectomy.

Given the effects of several immunosuppressive therapies, associations between such therapies and the RST should be discussed. Almost all of the included patients received immunosuppressive treatment prior to surgery; however, their medical therapy failed, resulting in colectomy. It is difficult to envision that immunosuppressive treatment, with the exception of enema therapy, was effective in only the rectal segment. If immunosuppressive treatment had been effective, patients would have exhibited improved symptoms and would not have required surgery, and endoscopy would also have revealed remission in not only the rectum but also the entire colonic area.

Regarding the definition of the RST, we used surgical specimens or endoscopic findings from shortly before surgery to assess patients treated via colectomy alone.

**Table 2** Univariate analysis for risk factors associated with Emergent/Urgent surgery

| Risk factors                        | urgent/emergent surgery n = 131 | elective surgery n = 351 | p-value | OR (95%CI) |
|-------------------------------------|----------------------------------|--------------------------|---------|------------|
| Gender male                         | 88(67.1)                         | 228(64.9)                | 0.64    | 1.10 (0.72-1.69) |
| Age at initial surgery < 44 years   | 80(61.1)                         | 158(45.0)                | <0.01*  | 1.92 (1.28-2.89) |
| Age at onset of UC < 32 years       | 55(41.9)                         | 181(51.6)                | 0.06    | 0.68 (0.45-1.02) |
| Duration of disease < 70 months     | 105(80.2)                        | 136(38.7)                | <0.01*  | 6.38 (3.95-10.32) |
| Severe/Fulminant disease            | 118(90.1)                        | 27(7.7)                  | <0.01*  | 108.9 (56.3-2227.1) |
| Rectal sparing type                 | 24(18.3)                         | 22(6.3)                  | <0.01*  | 3.35 (1.81-6.26) |
| Total given PSL dose <5000 mg       | 91(69.5)                         | 132(37.6)                | <0.01*  | 3.77 (2.46-5.80) |
| Daily pre-operative PSL dose \( \geq 9 \) mg/day | 103(78.6)                        | 139(39.6)                | <0.01*  | 5.61 (3.55-9.11) |
| Immunomodulators                    |                                  |                          |         |            |
| TAC/CsA                             | 39(29.8)                         | 84(23.9)                 | 0.19    | 1.35 (0.86-2.09) |
| AZA/6-MP                            | 16(12.2)                         | 108(30.8)                | <0.01*  | 0.32 (0.17-0.54) |
| Biologics administration            | 33(25.2)                         | 194(55.3)                | 0.72    | 1.08 (0.68-1.72) |

OR = Odds Ratio; CI = Confidence Interval; PSL = Prednisolone; TAC = Tacrolimus; CsA = Cyclosporine; AZA = Azathioprine 6-MP = 6-Mercaptopurine

Data are numbers with percentages in parentheses unless otherwise indicated

\*p < 0.05 (Significantly different)
Table 3 Multivariate analysis for risk factors associated with urgent/emergent surgery

| Risk Factors                           | OR(95% CI)   | p-value |
|----------------------------------------|--------------|---------|
| Age at initial surgery <44 years       | 1.94(0.93-4.17) | 0.08   |
| Duration of disease(month) ≤ 70 months | 2.45(1.10-5.54) | 0.03*  |
| Severe/Fulminant disease               | 87.1(40.9-205.1) | <0.01* |
| Total given PSL dose <5000 mg          | 3.02(1.39-6.76) | <0.01* |
| Daily pre-operative PSL dose ≥9 mg/day | 2.59(1.20-5.65) | 0.02*  |
| Immunomodulators administration (AZA/6-MP) | 0.68(0.26-1.69) | 0.41   |
| Rectal sparing type                    | 5.59(1.90-16.9) | <0.01* |

OR = Odds Ratio; CI = Confidence Interval.
PSL = Prednisolone; AZA = Azathioprine; 6-MP = 6-Mercaptopurine
*p < 0.05 (Significantly different)

Although diagnosis of the RST was defined as relatively reduced or no inflammation of the rectum compared to proximal colitis, Joo and Odze [19] reported that all RST patients were classified as having a relative RST, which indicates the existence of histological inflammation, even to a mild degree. Additionally, those researchers observed no correlations between the endoscopic findings and the colectomy histological findings [19]. They concluded that absolute rectal sparing does not occur in UC, even after the long-term use of anti-inflammatory medications [19]. In this series, histological inflammation of the rectum was also defined in all RST patients; however, the inflammation was relatively mild compared to that of the proximal colon. We also conjecture that degrees of inflammation may be difficult to classify via histological findings alone or that most such findings may be classified as indicative of inflamed mucosa. Therefore, we considered the diagnosis and definition of RST as adequate, despite the limitations mentioned below.

Some limitations were present in this study. First, this was a retrospective study with small number of patients from a single center. Multicenter and prospective cohort studies are needed. Second, the indications for urgent surgery were slightly vague. The selection and duration of conservative treatments for refractory disease before surgery, the timing of urgent surgery, or the decision to perform surgery may differ among patients, institutions, physicians, or surgeons. Third, although we believe that our definition was adequate, the definition of the RST was slightly vague. The distinction was often difficult and might be inappropriate in patients with boundary findings between 0 and 1 for the Mayo endoscopic score. The distinction of resected surgical specimens might also be inappropriate, given that the conditions were defined based on the subjective impression of surgeons and histologists.

Our results suggest that a shorter duration of colitis, a low dose of total PSL, a high dose of pre-operative PSL, severe disease, and the RST are risk factors for urgent/emergent surgery. These results may reveal a lack of response to pharmacotherapies for treatment of the RST, or these patients may develop more extensive and rapid unresponsiveness to pharmacotherapies. Therefore, we should be aware that patients with an initial onset of UC whose colitis exhibits the RST and worsens within a short period may have a higher risk for further surgical intervention.

Conclusion
The RST of UC was an independent risk factor for urgent/emergent surgery based on an analysis of surgically treated UC patients. Although the developmental mechanism and clinical significance of the RST remain unclear, these findings may suggest the need for a future colectomy, disease refractoriness, and pharmacotherapy resistance.

Abbreviations
UC: Ulcerative colitis; RST: Rectal-sparing type; PSL: Prednisolone; PSC: Primary sclerosing cholangitis; EIMs: Extra-intestinal manifestations; TAC: Tacrolimus; CsA: Cyclosporine; AZA: Azathioprine; 6-MP: 6-Mercaptopurine; IPAA: ileal pouch anal anastomosis; OR: Odds ratio; CI: Confidence interval

Acknowledgments
None

Funding
The authors declare that they had no sources of funding for this work.

Availability of data and materials
The data sets supporting the conclusions of this article are included within the article.
Data are available from the corresponding author upon reasonable request.

Authors’ contributions
YH was the lead author and conceived this study. MU contributed to data analysis and the writing of the article. TB, TC, HS and AH collected data and performed analysis. YT and HI performed analysis and reviewed the paper. All authors approved the final version of the manuscript.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
Not applicable

Ethics approval and consent to participate
This retrospective study was approved by the ethical board of Hyogo College of Medicine and was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all individuals included in the study.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.
References

1. Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut. 2006;55:749–53. doi:10.1136/gut.2005.062909.
2. Robert ME, Skacel M, Ullman T, Bernstein CN, Easley K, Goldblum JR. Patterns of colonic involvement at initial presentation in ulcerative colitis: a retrospective study of 46 newly diagnosed cases. Am J Clin Pathol. 2004;122:94–9. doi:10.1309/xkk-j84c-3jcw-3rc.
3. Swan NC, Geoghegan JG, O’Donoghue DP, Hyland JM, Sheahan K. Fulminant colitis in inflammatory bowel disease: detailed pathologic and clinical analysis. Dis Colon Rectum. 1998;41:1511–5. doi:10.1007/bf02237298.
4. Bjarnason I, Hayee B, Pavlidis P, Kvasnovsky C, Scalori A, Sisson G, et al. Review article: colorectal neoplasia in patients with primary sclerosing cholangitis and autoimmune sclerosing cholangitis. EBioMed. 2015;2:1523–7. doi:10.1067/j.ebiom.2015.08.041.
5. Tsaitas C, Semertzidou A, Sinakos E. Update on inflammatory bowel disease in patients with primary sclerosing cholangitis. World J Hepatol. 2014;6:178–87. doi:10.4254/wjh.v6i4.178.
6. Sinakos E, Samuel S, Enders F, Loftus EV Jr, Sandborn WJ, Lindor KD. Inflammatory bowel disease in patients with primary sclerosing cholangitis: a robust yet changing relationship. Inflamm Bowel Dis. 2013;19:1004–9. doi:10.1097/mib.0b013e3182802893.
7. Loftus EV Jr, Harewood GC, Loftus CG, Tremaine WJ, Harmsen WS, Zinner MJ, et al. PSC-IBD: a unique form of inflammatory bowel disease associated with primary sclerosing cholangitis. Gut. 2005;54:91–6. doi:10.1136/gut.2004.046615.
8. Torres J, Pineton de Chambrun G, Itzkowitz S, Sachar DB, Colombel JF. Review article: colorectal neoplasia in patients with primary sclerosing cholangitis and inflammatory bowel disease. Aliment Pharmacol Ther. 2011;34:687–508. doi:10.1111/j.1365-2036.2011.04753.x.
9. Seo M, Okada M, Osamura R, Haru S, Umeno T, Maehiro K, et al. Colon cancer in a patient with primary sclerosing cholangitis and long-standing ulcerative colitis. J Gastroenterol. 1997;32:83–8. doi:10.1007/BF01213301.
10. Pavlidis M, Cleland J, Rahman M, Christian A, Doyle J, Gaunt R, et al. Outcomes after ileal pouch anal anastomosis in patients with primary sclerosing cholangitis. J Crohns Colitis. 2014;8:666–70. doi:10.1016/j.crohns.2013.12.007.
11. Glickman JN, Bousvaros A, Farraye FA, Zholudev A, Friedman S, Wang HH, et al. Pediatric patients with untreated ulcerative colitis may present initially with unusual morphologic findings. Am J Surg Pathol. 2004;28:190–5. doi:10.1016/j.aps.2004.02.006.
12. Washington K, Greenston JK, Montgomery E, Shyr Y, Crissinger KD, Polk DB, et al. Histopathology of ulcerative colitis in initial rectal biopsy in children. Am J Surg Pathol. 2002;26:1441–9. doi:10.1097/00000478-200211000-00006.
13. Rajvial SR, Puntis JW, McClean P, Davison SM, Newell SJ, Sugarman I, et al. Endoscopic rectal sparing in children with untreated ulcerative colitis. J Pediatr Gastroenterol Nutr. 2004;39:66–9. doi:10.1097/00000478-200401000-00015.
14. Aloiz M, D’Arcangelo G, Pofil T, Vlassallo R, Rizzo V, Nuti F, et al. Presenting features and disease course of pediatric ulcerative colitis. J Crohns Colitis. 2013;7:e509–15. doi:10.1016/j.crohns.2013.03.007.
15. Oshihana N, Kitano A, Nakamura S, Obata A, Hashimura H, Hiki M, et al. Clinical and prognostic features of rectal sparing in ulcerative colitis. Digestion. 1989;49:39–43. doi:10.1159/000199823.
16. Trueove SC, Wits L. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955;2:1041–8. doi:10.1136/bmj.2.4947.1041.
17. Kim B, Barnett JJ, Kleer CG, Appelman HD. Endoscopic and histological patchiness in treated ulcerative colitis. Am J Gastroenterol. 1999;94:3258–62. doi:10.1111/j.1572-0241.1999.01533.x.
18. Park SH, Yang SK, Park SK, Kim JW, Yang DH, Jung KW, et al. Atypical distribution of inflammation in newly diagnosed ulcerative colitis is not rare. Can J Gastroenterol Hepatol. 2014;28:125–30. doi:10.1155/2014/834512.
19. Joo M, Odze RD. Rectal sparing and skip lesions in ulcerative colitis: a comparative study of endoscopic and histologic findings in patients who underwent proctocolectomy. Am J Surg Pathol. 2010;34:689–96. doi:10.1097/PAS.0b013e3181db84cd.