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Clinical features and differential diagnosis in symptomatic localized terminal ileitis or ulcer

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Abstract

Despite advancements in diagnostic techniques, the accurate identification and management of localized terminal ileitis or ulcers (LTIU) remains challenging, with a wide range of associated diseases presenting with similar clinical and endoscopic features. This retrospective observational study aimed to determine the etiology and discrimination of various diseases in patients with symptomatic LTIU. Data on demographics, clinical manifestations, and endoscopic findings were collected and analyzed statistically using descriptive and inferential methods, including frequency analysis and chi-square tests. Among the 224 patients who underwent LTIU on ileocolonoscopy, 110 (49.1%) had symptoms, of which 71 (64.5%) had specific etiologies on initial testing and after 6 months of follow-up. Definitive diagnoses were ascertained, with Crohn disease (CD) and Behçet disease (BD) being the most common diseases in this cohort, accounting for 27.3% (30 patients) and 18.2% (20 patients) of cases, respectively. Other diagnoses included infectious enteritis in 10 (9.1%) patients, drug-induced enteropathy in 5 (4.5%), intestinal tuberculosis in 5 (4.5%), and lymphoma in 1 (0.9%). Additionally, 39 patients (35.5%) had nonspecific ulcers. After 1 year of treatment, symptomatic and endoscopic resolution was noted in 7 out of 30 patients (23.3%) with CD and 10 out of 20 (50.0%) with BD. Of the 39 patients initially diagnosed with nonspecific ulcers with persistent symptoms, 2 were eventually diagnosed with CD. The high proportion of diagnosed diseases among symptomatic patients with LTIU underscores the importance of early and accurate diagnosis in guiding appropriate treatment strategies. These findings highlight the need for further research to refine diagnostic approaches and optimize patient outcomes in this challenging clinical scenario.

Abbreviations: BD = Behçet disease, CD = Crohn disease, CI = confidence interval, CRP = C-reactive protein, EIM = extraintestinal manifestation, GI = gastrointestinal, Hb = hemoglobin, IRB = institutional review board, ITB = intestinal tuberculosis, LTIU = localized terminal ileitis or ulcers, NSAID = non-steroidal anti-inflammatory drug, SPSS = statistical package for the social sciences.

Keywords: Behçet disease, Crohn disease, differential diagnosis, epidemiology, ileal ulcer, ileitis

1. Introduction

Inflammation and ulceration in the terminal ileum are often observed as colonoscopies increase. Ileal inflammation and ulcers have been observed in patients with Crohn disease (CD), Behçet disease (BD), intestinal tuberculosis (ITB), drug-induced enteropathy, infectious enteritis, nonspecific ileitis, etc. Localized terminal ileitis or ulcers (LTIU) in asymptomatic individuals usually resolve without treatment, and most cases do not progress.[1,2] However, there are a little evidence in the literature regarding the clinical outcomes of symptomatic LTIU, particularly in association with diseases such as CD and BD. Some diseases may be diagnosed early because of their history, clinical symptoms, endoscopic features, and laboratory findings.[3] A definitive diagnosis was made during follow-up. Given the limited evidence available regarding the clinical outcomes of symptomatic LTIU, there is a pressing need to better understand the etiology and discriminatory ability of various diseases in these patients to guide optimal diagnostic and treatment strategies. Therefore, in this study, we evaluated the etiology and discriminatory ability of various diseases in patients with symptomatic LTIU.

2. Methods

We analyzed the medical and endoscopic records of symptomatic patients aged ≥19 years who were diagnosed with LTIU

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study was approved by the Ethics Committee of the Pusan National University Yangsan Hospital Institutional Review Board (No. 55-2024-042). Written informed consent was obtained from all patients.

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through ileocolonoscopic examination at the Pusan National University Yangsan Hospital, a referral hospital in Yangsan, South Korea, from January 2018 to October 2023. Data collected from patients' records, including their demographic and endoscopic features, were analyzed. Initial ileocolonoscopic photographs were reviewed by 3 authors (KWJ, JJO, and PSB) who were blinded to the clinical course of the patients. The study protocol received approval from our center Institutional Review Board (no. 55-2024-042).

2.1. Definitions

2.1.1. Symptomatic LTIU. Symptomatic LTIU was defined as localized involvement of the terminal ileum presenting with inflammation, superficial ulcers, or deep ulcers without colonic mucosal involvement and symptoms such as abdominal pain, gastrointestinal (GI) bleeding, diarrhea, weight loss, oral ulcers, or fever.

2.1.2. Crohn disease. CD was diagnosed according to the European Crohn and Colitis Organization consensus based on a combination of clinical manifestations and endoscopic and histological evidence.[4]

2.1.3. Behçet disease. BD was diagnosed based on the International Study Group of Behçet Disease and the International Criteria for Behçet Disease.[5,6]

2.1.4. Intestinal tuberculosis. The diagnosis of ITB was made based on the patient characteristic clinical, endoscopic, and histological features (presence of granulomas) or microbiological tests (presence of acid-fast bacilli on smear examination or culture).

2.2. Statistical analyses

Categorical variables are described in terms of frequency and percentage, while numerical variables are defined in terms of median or mean ± standard deviation. Statistical differences between groups were tested using the Kruskal–Wallis and chi-square tests with the calculation of the 95% confidence interval. A two-tailed probability value (P value) <.05 was considered statistically significant. All statistical calculations were performed using Statistical Package for the Social Sciences (SPSS, Inc., Chicago) version 15 for Microsoft Windows (Microsoft Corp., Redmond). We conducted post hoc testing for within-group significance among the 6 groups using the Mann–Whitney U test, followed by the application of the Bonferroni correction to identify significant groups.

3. Results

3.1. Baseline characteristics

We identified 224 patients with LTIU who underwent ileocolonoscopy. Among them, 114 patients without symptoms, colonic lesions, or aged <18 years were excluded (Fig. 1). The remaining 110 patients in this study comprised 74 men and 36 women, with a mean age of 46.47 years (range: 19 – 80 years). The 4 most prevalent symptoms were abdominal pain (56.4%), diarrhea (33.6%), oral ulcer (27.3%), and weight loss (16.4%). Ileocolonoscopy revealed ulcers among 110 patients; 101 (91.8%) showed ulcers, and 9 (8.2%) had only ileitis. Ulcers with a size of ≥1 cm accounted for 49 (48.5%), and multiple ulcers were observed in 58 (57.4%) cases. Superficial and deep ulcers were recorded in 73 (72.3%) and 28 (27.7%) patients, respectively. Discrete margins were observed in 44 (43.6%) patients, while irregular margins were seen in 57 (56.4%). Additionally, nodularity was present in 27 (24.6%) patients, edema in 46 (41.8%), erosion in 72 (66.1%), and strictures in 35 (31.8%) Table 1.

3.2. Clinical features according to etiology

Among the participants, 71 (64.5%) received specific diagnoses. Final diagnoses included CD (30 patients), BD (20 patients), infectious enteritis (10 patients), drug-induced enteropathy (5 patients), ITB (5 patients), and lymphoma (1 patient) Table 2.

Regarding clinical presentation, significant differences were observed in abdominal pain, oral ulcers, and genital ulcers (P = .004, P = .000, and P = .003, respectively) between the groups. Additionally, hemoglobin (Hb) and C-reactive protein (CRP) levels showed significant differences (P = .015 and .016, respectively). post hoc analysis of laboratory findings revealed significant differences in Hb (P = .002) and CRP levels (P = .001) between the BD group and other groups, with lower Hb and higher CRP levels observed in the BD group.

3.3. Ileocolonoscopic features according to etiology

Significant differences were observed in the ulcer size, number, margin, edema, erosion, and stricture variables (Table 3). First, concerning ulcer size, a significant difference existed between each group, with many ulcers larger than 1 cm in the BD and ITB groups and many ulcers smaller than 1 cm in the unknown

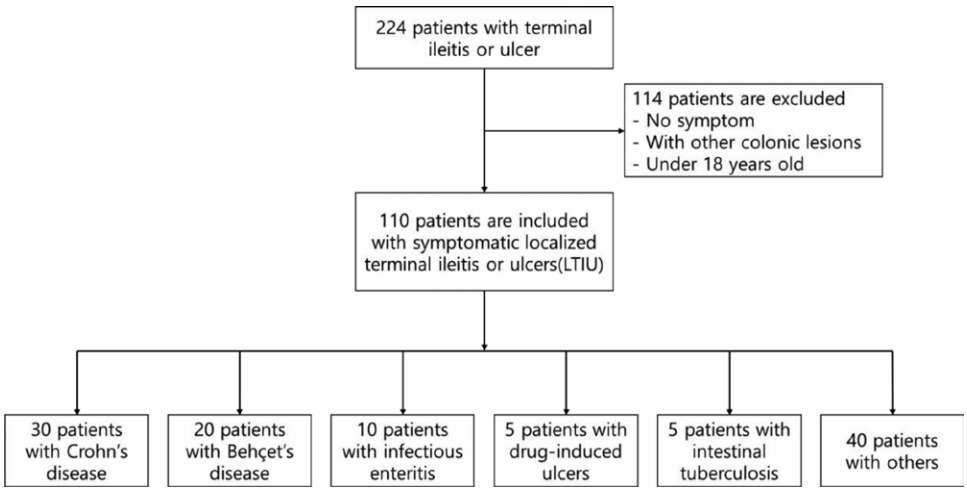

Figure 1. Flowchart of the inclusion of patients with symptomatic localized terminal ileal ulcers.

Table 1

Baseline characteristics, clinical, and endoscopic features of patients with localized terminal ileitis and ulcers (n = 110).

Age, years (mean ± SD)	**46.47 ± 17.95**
Gender, n (male: female)	74:36 (67.3%:32.7%)
Duration of follow-up, months (median [IQR])	12.6 [6.1;26.7]
Clinical features, n (%)	
Abdominal pain	62 (56.4%)
Diarrhea	37 (33.6%)
Constipation	8 (7.3%)
Weight loss	18 (16.4%)
GI bleeding	26 (23.6%)
Fever	11 (10%)
Oral ulcer	30 (27.3%)
Genital ulcer	5 (4.5%)
Laboratory findings, mean ± SD/median [IQR]	
WBC	7.43 ± 3.24
	6.72 [5.46;8.76]
Hb	13.27 ± 2.12
	13.60 [12.20;14.70]
Albumin	4.25 ± 0.48
	4.30 [4.00;4.50]
CRP	1.92 ± 4.24
	0.28 [0.09;1.70]
Ileocolonoscopic features, n (%)	
Ulcer	
Ulcer	101 (91.8%)
Ileitis	9 (8.2%)
Ulcer size	
<1 cm	52 (51.5%)
≥1 cm	49 (48.5%)
Ulcer number	
Single	43 (42.6%)
Multiple	58 (57.4%)
Superficial/Deep	
Superficial	73 (72.3%)
Deep	28 (27.7%)
Margin	
Discrete	44 (43.6%)
Irregular	57 (56.4%)
Nodularity	27 (24.6%)
Edema	46 (41.8%)
Erosion	72 (66.1%)
Stricture	35 (31.8%)

CRP = C-reactive protein, GI = gastrointestinal, Hb = hemoglobin, IQR = interquartile range, SD = standard deviation, WBC = white blood cell.

groups (P = .000). Second, significant differences were noted in the number of ulcers in the ileum; single ulcers were more common in the BD group, while multiple ulcers were observed more frequently in the CD or infectious and unknown groups (P = .002). Regarding ulcer depth, most groups had superficial ulcers; however, deep ulcers were more prevalent in the BD group (P = .000). Regarding the variable of margin, the CD, infectious, and ITB groups relatively exhibited irregular margins (P = .033). Regarding edema, the CD and ITB groups showed many edematous lesions, while BD showed no edematous lesion, indicating a significant difference (P = .000). Although most lesions did not exhibit nodularity; however, CD and ITB lesions displayed a considerable amount of nodularity (P = .001). The erosion variable also showed a significant difference, with relatively fewer erosions observed in the BD group (P = .000). Finally, the CD and ITB groups showed a relatively prevalence of strictures (P = .004) Table 3.

3.4. Clinical features according to CD, BD, and others

To confirm if characteristic findings are observed for CD and BD, we grouped infectious, drug-induced, ITB, and unknown cases as "Others" and compared CD and BD to others (Table 4). Similar to the results shown in Table 2, abdominal pain, oral ulcers, and genital ulcers showed significant differences (P = .010, P = .000, and P = .000, respectively). Additionally, significant differences were observed in the incidence of diarrhea, which was more frequently observed in patients with CD (P = .033). Similar to the results in Table 2, significant differences were observed in Hb and CRP levels (P = .012 and P = .002, respectively). Ileocolonoscopy also exhibited significant differences in ulcer size, number, superficial edema, nodularity, and erosion. Among the 3 groups, the BD group showed a higher prevalence of single ulcer, ulcer size (>1 cm) and deep ulcers (P = .000, P = .000, and P = .000, respectively). In the BD group, edema, nodularity, and erosion were relatively less frequent (P = .000, P = .000, and P = .000, respectively). A total of 30 patients with CD were enrolled in this study, with a mean age of 34.6 years (range, 19–80 years), and 22 (73.3%) were male. 9 had perianal disease, and 5 exhibited extraintestinal manifestations (EIM). The EIMs included skin lesions in 2 patients, arthritis in 2 patients, and osteoporosis in 1 patient. Following 1 year of treatment with immunomodulators and steroids, symptomatic and endoscopic resolution was noted in 7 patients (23.3%) with CD. Over an average follow-up period of 15 months, mucosal healing was observed in 14 patients (46.7%), while recurrence occurred in 5 (35.7%). Additionally, 20 patients with BD were included in this study, with a mean age of 51.7 years (range: 34–80), and 11 (55.0%) were male. Following 1 year of treatment with immunomodulators and steroids, symptomatic and endoscopic resolution was noted in 10 patients (50.0%) with BD. Over an average follow-up period of 33 months, mucosal healing was observed in 13 patients (65.0%), while recurrence occurred in 3 (23.1%) Table 4.

4. Discussions

Terminal ileitis or ulcer refers to inflammation or ulcers of the distal portion of the ileum and ileocecal valve. These lesions can be detected in both asymptomatic and symptomatic patients. The incidental detection of LTIU in asymptomatic cases is relatively uncommon, occurring in 1.6% of patients. In contrast, a much larger proportion, ranging from 2% to 7%, of symptomatic patients undergoing colonoscopy may show such abnormalities.[7] The significance of these abnormalities in asymptomatic patients is relatively low, and they often have a good prognosis.[8] Mild ileitis with a few aphthous ulcers can be found incidentally, but it does not have an apparent cause and remains indeterminate despite ileal biopsies.[9] Additionally, the rate of progression to overt CD is low, and watchful waiting may be a reasonable strategy.[7]

In contrast, the chances of finding a specific etiology are much higher in symptomatic patients.[10] The clinical presentation can vary but often includes abdominal pain, diarrhea, weight loss, fever, and occasionally, obstructive symptoms. On ileocolonoscopy, LTIU appeared similar; however, upon closer observation, it may be possible to estimate specific etiologies depending on the direction (longitudinal vs transverse), margin (discrete vs irregular), depth (superficial vs deep), and number (single vs multiple) of ulcers (Fig. 2). Despite improvements in diagnosis and therapy, there are almost no specific guidelines for the diagnosis and treatment of symptomatic terminal ileitis.[11] Such LTIU may result from non anti-inflammatory drug (NSAID) intake or other pathological conditions, such as CD, BD, infection, lymphoid hyperplasia, and lymphoma. A recent retrospective study from Türkiye reported the following findings among 398 patients: CD was identified in 16.6%, NSAID-induced ulcers in 14.6%, ASA-related ulcers in 7.0%, ITB in 1.0%, BD in 0.5% and nonspecific ulcers in 53.3%.[12] One study showed that 55.4% of patients had specific etiologies on initial testing, and after 3 to 6 months of follow-up, 59.5% were definitively

Table 2

Clinical presentation and laboratory findings.

	Diagnosis						
	CD	BD	Infectious	Drug	ITB	Unknown	*P*
Clinical presentation							
Abdominal pain							.004*
Presence	21 (70.0%)	15 (75.0%)	8 (80.0%)	2 (40.0%)	1 (20.0%)	15 (37.5%)	
Absence	9 (30.0%)	5 (25.0%)	2 (20.0%)	3 (60.0%)	4 (80.0%)	25 (62.5%)	
Fever							.117*
Presence	3 (10.0%)	4 (20.0%)	2 (20.0%)	0 (0.0%)	1 (20.0%)	1 (2.5%)	
Absence	27 (90.0%)	16 (80.0%)	8 (80.0%)	5 (100.0%)	4 (80.0%)	39 (97.5%)	
Weight loss							.319*
Presence	9 (30.0%)	2 (10.0%)	1 (10.0%)	0 (0.0%)	1 (20.0%)	5 (12.5%)	
Absence	21 (70.0%)	18 (90.0%)	9 (90.0%)	5 (100.0%)	4 (80.0%)	35 (87.5%)	
Constipation							.194*
Presence	0 (0.0%)	1 (5.0%)	1 (10.0%)	0 (0.0%)	1 (20.0%)	5 (12.5%)	
Absence	30 (100.0%)	19 (95.0%)	9 (90.0%)	5 (100.0%)	4 (80.0%)	35 (87.5%)	
Diarrhea							.077*
Presence	15 (50.0%)	3 (15.0%)	4 (40.0%)	0 (0.0%)	1 (20.0%)	14 (35.0%)	
Absence	15 (50.0%)	17 (85.0%)	6 (60.0%)	5 (100.0%)	4 (80.0%)	26 (65.0%)	
GI bleeding							.123*
Presence	6 (20.0%)	4 (20.0%)	3 (30.0%)	4 (80.0%)	1 (20.0%)	8 (20.0%)	
Absence	24 (80.0%)	16 (80.0%)	7 (70.0%)	1 (20.0%)	4 (80.0%)	32 (80.0%)	
Oral ulcer							.000*
Presence	5 (16.7%)	19 (95.0%)	3 (30.0%)	0 (0.0%)	0 (0.0%)	3 (7.5%)	
Absence	25 (83.3%)	1 (5.0%)	7 (70.0%)	5 (100.0%)	5 (100.0%)	37 (92.5%)	
Genital ulcer							.003*
Presence	0 (0.0%)	5 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Absence	30 (100.0%)	15 (75.0%)	10 (100.0%)	5 (100.0%)	5 (100.0%)	40 (100.0%)	
Laboratory findings							
WBC	7.58 [6.20;9.70]	5.85 [4.77;9.68]	7.55 [6.18;8.67]	5.06 [4.66;6.69]	6.41 [5.98;8.23]	6.40 [5.25;8.17]	.053
Hb	13.90 [12.50;14.90]^{AB}	12.70 [11.20;13.35]^{B}	14.15 [13.00;14.90]^{AB}	10.70 [10.50;12.60]^{AB}	14.20 [13.00;15.10]^{AB}	13.85 [12.65;15.25]^{A}	.015
Albumin	4.20 [3.90;4.60]	4.20 [3.95;4.30]	4.30 [4.00;4.70]	4.30 [3.80;4.30]	4.60 [4.00;4.60]	4.40 [4.20;4.60]	.165
CRP	0.41 [0.12;1.73]^{AB}	1.32 [0.32;4.46]^{A}	0.09 [0.05;6.51]^{AB}	0.30 [0.13;0.72]^{AB}	0.14 [0.11;0.44]^{AB}	0.11 [0.06;0.34]^{B}	.016

A, B, AB: post hoc test results, Bonferroni correction.

BD = Behcet disease, CD = Crohn disease, CRP = C-reactive protein, GI = gastrointestinal, Hb = hemoglobin, ITB = intestinal tuberculosis, WBC = white blood cell.

*Fisher's exact test.

Table 3

Ileocolonoscopic features according to etiology.

	Diagnosis						
	CD	BD	Infectious	Drug	ITB	Unknown	*P*
Ulcer size							.000*
<1 cm	15 (51.7%)	2 (10.5%)	5 (55.6%)	2 (50.0%)	1 (20.0%)	27 (77.1%)	
≥1 cm	14 (48.3%)	17 (89.5%)	4 (44.4%)	2 (50.0%)	4 (80.0%)	8 (22.9%)	
Ulcer No.							.002*
Single	6 (20.7%)	15 (78.9%)	3 (33.3%)	2 (50.0%)	3 (60.0%)	14 (40.0%)	
Multiple	23 (79.3%)	4 (21.1%)	6 (66.7%)	2 (50.0%)	2 (40.0%)	21 (60.0%)	
Superficial							.000*
Superficial	26 (89.7%)	3 (15.8%)	8 (88.9%)	2 (50.0%)	4 (80.0%)	30 (85.7%)	
Deep	3 (10.3%)	16 (84.2%)	1 (11.1%)	2 (50.0%)	1 (20.0%)	5 (14.3%)	
Margin							.033*
Discrete	8 (27.6%)	11 (57.9%)	3 (33.3%)	2 (50.0%)	0 (0.0%)	20 (57.1%)	
Irregular	21 (72.4%)	8 (42.1%)	6 (66.7%)	2 (50.0%)	5 (100.0%)	15 (42.9%)	
Edema							.000*
Presence	22 (73.3%)	0 (0.0%)	2 (20.0%)	2 (40.0%)	4 (80.0%)	16 (40.0%)	
Absence	8 (26.7%)	20 (100.0%)	8 (80.0%)	3 (60.0%)	1 (20.0%)	24 (60.0%)	
Nodularity							.001*
Presence	15 (50.0%)	1 (5.0%)	2 (20.0%)	0 (0.0%)	3 (60.0%)	6 (15.0%)	
Absence	15 (50.0%)	19 (95.0%)	8 (80.0%)	5 (100.0%)	2 (40.0%)	34 (85.0%)	
Erosion							.000*
Presence	22 (75.9%)	3 (15.0%)	7 (70.0%)	5 (100.0%)	4 (80.0%)	31 (77.5%)	
Absence	7 (24.1%)	17 (85.0%)	3 (30.0%)	0 (0.0%)	1 (20.0%)	9 (22.5%)	
Stricture							.004*
Presence	14 (46.7%)	7 (35.0%)	4 (40.0%)	1 (20.0%)	4 (80.0%)	5 (12.5%)	
Absence	16 (53.3%)	13 (65.0%)	6 (60.0%)	4 (80.0%)	1 (20.0%)	35 (87.5%)	

BD = Behcet disease, CD = Crohn disease, ITB = intestinal tuberculosis.

*Fisher's exact test.

diagnosed with 25.7% diagnosed with CD, 14.9% with NSAID-induced ulcers, 12.2% with ITB, and 6.8% with eosinophilic enteritis. Additionally, 40.5% of patients were found to have nonspecific ulcers.[13]

The primary goal of our study was to determine whether the disease could be distinguished based on clinical symptoms, blood tests, and endoscopic findings in patients with symptomatic LTIU.

In our study, 64.5% of patients were ultimately diagnosed, and CD (27.3%) and BD (18.2%) were common diseases observed. Therefore, patients with symptomatic LTIU in South Korea should be evaluated for CD and BD. CD can affect any part of the GI tract, but the terminal ileum is most frequently affected. In CD, ulcers vary from small aphthous ulcerations to multiple, irregularly shaped ulcerations, with discontinuous distribution of longitudinal ulcers (defined as ≥4 to 5 cm), cobblestone appearance, or small aphthous ulcerations arranged longitudinally. However, in BD, a round shape, fewer numbers (≤5), focal distribution, discrete borders, and deep penetration are the most common manifestations, with some patients having multiple ulcerations. BD is an idiopathic inflammatory disease characterized by varying degrees of vasculitis. Common symptoms include recurrent oral and genital ulcers and ocular and skin lesions. The prevalence of BD is highest in East Asia, including South Korea. Intestinal BD occurs in 3% to 60% of patients with BD, with a higher frequency of GI involvement in East Asian countries.[14] There are no pathognomonic laboratory tests or endoscopic findings of intestinal BD, although a few large and deep ulcerations with discrete borders have been described as characteristic endoscopic patterns. Cheon et al defined the diagnostic criteria for intestinal BD in Korean patients with ileocolonic ulcers based on endoscopic features (typical or atypical intestinal BD ulcerations) and clinical patterns (systemic symptoms, oral ulcerations, or EIMs).[15] Deep punched-out ulcers, such as severe bleeding and perforation, are the most common intestinal complications. Intestinal lesions are considered a poor prognostic factor.[16] Because intestinal BD shares many characteristics with CD, the differential diagnosis of intestinal BD and CD is challenging. Weight loss and anal lesions are associated with CD, while oral and genital ulcers are more common in patients with BD.

In our study, abdominal pain, diarrhea, oral ulcers, and genital ulcers showed significant differences in clinical findings, indicating that these are relatively more frequently observed in CD and BD and may manifest as clinical patterns. Abdominal pain is the main symptom common in CD and BD. Diarrhea was relatively common in patients with CD, whereas oral and genital ulcers were more common in patients with BD. Although there might be a selection bias where patients with BD tend to have more severe disease and patients with CD less severe, patients with BD showed relatively lower Hb and higher CRP levels, indicating that certain pathological features of BD may be reflected in specific laboratory tests. In patients with CD involving only the terminal ileum, inflammatory markers may be lower due to the localized nature of the disease. Additionally, significant differences were observed in the endoscopic findings between patients with CD and those with BD. Specifically, in the case of BD, noticeable differences were observed in terms of size, number, depth, edema, and nodularity compared to CD and the other groups.

Extrapulmonary tuberculosis occurs in 20% of patients with tuberculosis. Meanwhile, 10% of all cases of extrapulmonary tuberculosis are ITB. ITB can coexist with pulmonary TB, checking chest X-rays a valuable diagnostic tool. In this study, 3 out of 5 patients exhibited abnormalities on CXR. The gold standard examination for ITB is the culture of *Mycobacterium tuberculosis* using intestinal mucosal tissue specimens. However, the paucibacillary nature of these bacteria makes it difficult to detect *M. tuberculosis* utilizing this method, increasing the risk of false negatives.[17] In this study, the diagnosis of ITB was made using TB PCR in 4 patients and TB culture in 1 patient. After 6 months of anti treatment, all patients showed improvement with mucosal healing. Both CD and ITB showed similar features during colonoscopy and macroscopic examination. ITB

Table 4

CD versus BD versus others.

	Diagnosis			
	CD	BD	Others	*P*
Abdominal pain				.010
Presence	21 (70.0%)	15 (75.0%)	26 (43.3%)	
Absence	9 (30.0%)	5 (25.0%)	34 (56.7%)	
Fever				.216*
Presence	3 (10.0%)	4 (20.0%)	4 (6.7%)	
Absence	27 (90.0%)	16 (80.0%)	56 (93.3%)	
Weight loss				.083*
Presence	9 (30.0%)	2 (10.0%)	7 (11.7%)	
Absence	21 (70.0%)	18 (90.0%)	53 (88.3%)	
Constipation				.113*
Presence	0 (0.0%)	1 (5.0%)	7 (11.7%)	
Absence	30 (100.0%)	19 (95.0%)	53 (88.3%)	
Diarrhea				.033
Presence	15 (50.0%)	3 (15.0%)	19 (31.7%)	
Absence	15 (50.0%)	17 (85.0%)	41 (68.3%)	
GI bleeding				.788*
Presence	6 (20.0%)	4 (20.0%)	16 (26.7%)	
Absence	24 (80.0%)	16 (80.0%)	44 (73.3%)	
Oral ulcer				.000
Presence	5 (16.7%)	19 (95.0%)	6 (10.0%)	
Absence	25 (83.3%)	1 (5.0%)	54 (90.0%)	
Genital ulcer				.000*
Presence	0 (0.0%)	5 (25.0%)	0 (0.0%)	
Absence	30 (100.0%)	15 (75.0%)	60 (100.0%)	
WBC	7.58 [6.20;9.70]	5.85 [4.77;9.68]	6.54 [5.33;8.27]	.083
Hb	13.90 [12.50;14.90][AB]	12.70 [11.20;13.35][B]	13.90 [12.60;15.05][A]	.012
Albumin	4.20 [3.90;4.60]	4.20 [3.95;4.30]	4.30 [4.15;4.60]	.063
CRP	0.41 [0.12;1.73][A]	1.32 [0.32;4.46][A]	0.12 [0.06;0.43][B]	.002
Ulcer				.461*
Presence	29 (96.7%)	19 (95.0%)	53 (88.3%)	
Absence	1 (3.3%)	1 (5.0%)	7 (11.7%)	
Ulcer size				.000
<1 cm	15 (51.7%)	2 (10.5%)	35 (66.0%)	
≥1 cm	14 (48.3%)	17 (89.5%)	18 (34.0%)	
Ulcer No.				.000
Single	6 (20.7%)	15 (78.9%)	22 (41.5%)	
Multiple	23 (79.3%)	4 (21.1%)	31 (58.5%)	
Superficial				.000
Superficial	26 (89.7%)	3 (15.8%)	44 (83.0%)	
Deep	3 (10.3%)	16 (84.2%)	9 (17.0%)	
Margin				.087
Discrete	8 (27.6%)	11 (57.9%)	25 (47.2%)	
Irregular	21 (72.4%)	8 (42.1%)	28 (52.8%)	
Edema				.000
Presence	22 (73.3%)	0 (0.0%)	24 (40.0%)	
Absence	8 (26.7%)	20 (100.0%)	36 (60.0%)	
Nodularity				.000*
Presence	15 (50.0%)	1 (5.0%)	11 (18.3%)	
Absence	15 (50.0%)	19 (95.0%)	49 (81.7%)	
Erosion				.000
Presence	22 (75.9%)	3 (15.0%)	47 (78.3%)	
Absence	7 (24.1%)	17 (85.0%)	13 (21.7%)	
Stricture				.077
Presence	14 (46.7%)	7 (35.0%)	14 (23.3%)	
Absence	16 (53.3%)	13 (65.0%)	46 (76.7%)	

A, B, AB: post hoc test results, Bonferroni correction.

BD = Behcet disease, CD = Crohn disease, CRP = C-reactive protein, GI = gastrointestinal, Hb = hemoglobin, WBC = white blood cell.

*Fisher's exact test.

is characterized by isolated or a few ulcerations, transverse ulcers, nodular lesions, or fibrous strictures.[11,18–20] One of the most common causes is the ingestion of drugs such as NSAIDs, and a proper history is mandatory before launching a comprehensive investigation on the patient. In our study, the causes of drug-induced enteritis included anticoagulants/antiplatelets in 3 patients, NSAIDs in 1 patient, and MMF/tacrolimus in 1 patient. Based on their medical history, patients presenting with acute symptoms such as abdominal pain, vomiting, and fever were classified as infectious cases. The culture test results showed that *Clostridium perfringens* was identified in 1 patient, and *Clostridium difficile* GDH was detected in 3 patients: The remaining patients were presumed to have viral infectious diseases. Most infectious or nonspecific LTIU disappeared after

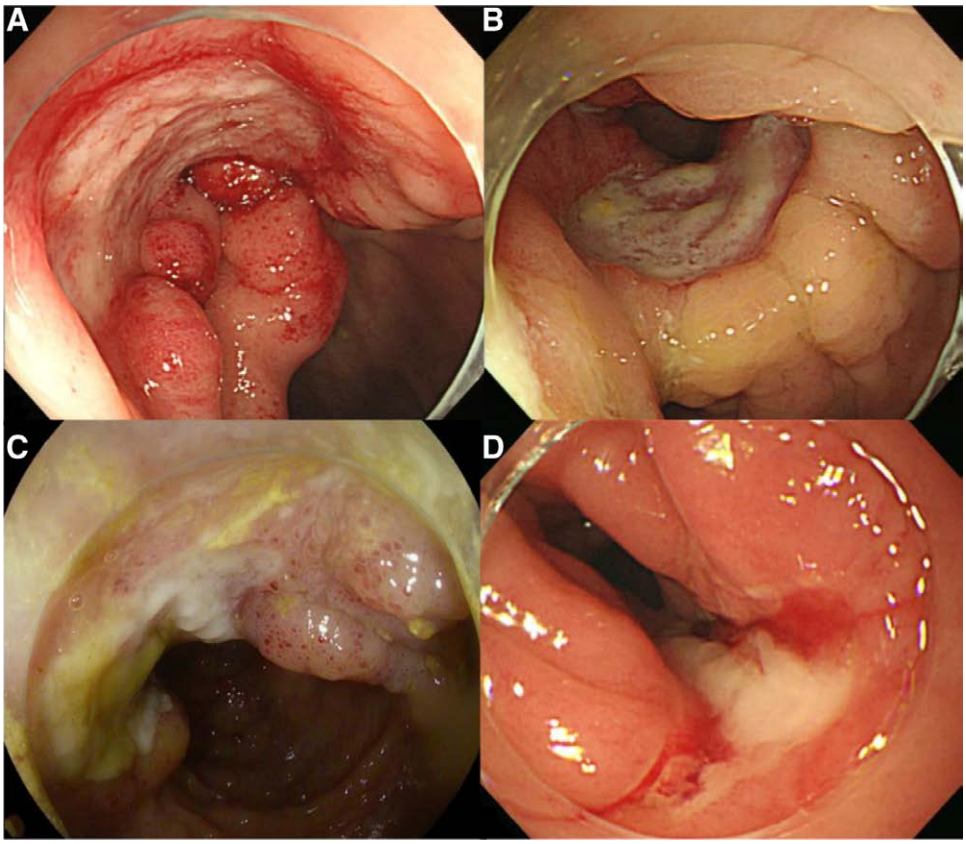

Figure 2. Endoscopic findings in patients with localized terminal ileitis and ulcer; (A, B) Behcet disease, (C, D) Crohn disease.

follow-up. Among the 39 patients diagnosed with nonspecific ulcers and persistent symptoms, 2 were later diagnosed with CD.

This study had some limitations. First, it was limited by its retrospective single-center design and the small number of patients with rare diseases. However, this is the first study to demonstrate that CD and BD are common causes of LTIU in South Korea. Second, radiological findings, histological results, and fecal calprotectin levels were excluded from our diagnostic criteria due to their limited applicability to a subset of patients. Although CT scans were performed on some patients, the majority showed normal findings. Histological examinations via biopsies were conducted for differential diagnosis, revealing inflammation in many cases. While biopsies can aid in diagnosing certain patients, a comprehensive assessment of medical history, clinical symptoms, and endoscopic findings often proves more crucial than relying on radiological or histological results.

5. Conclusion

In summary, our study aimed to identify diagnostic markers for distinguishing between different causes of LTIU. The clinical and endoscopic findings should alert the treating physician to thoroughly investigate for organic diseases such as CD, BD, or ITB. Carefully examining endoscopic findings and the patient medical history facilitates relatively easy diagnosis due to their differing endoscopic characteristics. This aids in understanding the typical appearance of each disease, thereby assisting in evaluating patients with LTIU. The discovery of an ulcer or ileitis in the terminal ileum during ileocolonoscopy in symptomatic patients dramatically increases the likelihood of accurate diagnosis. Additionally, even if an early diagnosis is not achieved, follow-up with colonoscopy can still aid in reaching a diagnosis. It enables targeted treatment through a focused approach to commonly diagnosed diseases.

Author contributions

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