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Original Article

Inflammatory Patterns of Crohn's Terminal Ileitis

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Abstract

Objective: Studies on terminal ileitis date back a long time. Crohn's disease primarily involves the terminal ileum though it may affect the entire gastrointestinal system with focal/patchy involvement. The aim of this study was to define the histopathologic features of terminal ileitis in detail in a cohort of Crohn's patients in an attempt to provide a simple guide for practicing pathologists. We further aimed to determine the inflammatory patterns of terminal ileitis in initial and posttreatment biopsies.

Methods: A total of 152 patients with a diagnosis of terminal ileitis of Crohn's disease were included in the study. Of them, 75 cases were initial biopsies (IB), and 77 patients were control biopsies (CB). Histopathological features of activity and chronicity were evaluated for each case.

Results: Sixty-four (42.1%) cases were female, and 88 (57.9%) were male. In the IB group, the number of patients with terminal ileitis, segmental colitis, and diffuse colitis was 39 (57.4%), 25 (36.8%) and 4 (5.8%), respectively; the number of patients in the CB group was found to be 36 (59%), 20 (32.8%), and 5 (8.2%). No significant difference was found about colonic involvement.

Conclusion: The present study was designed to emphasize the importance of detailed histopathologic examination of terminal ileum biopsies in a cohort of Crohn's disease patients. Chronicity features are seen at a similar rate between IB and CB. Therefore, our results suggest that chronic ileitis, characterized by patchy inflammation, either active or inactive, is the predominant inflammation pattern of Crohn's disease's terminal ileum, regardless of the time of the biopsy.

Keywords: Activity, chronicity, Crohn's disease, histopathology, terminal ileitis

INTRODUCTION

Terminal ileitis (TI) is defined as an inflammation of the terminal ileum, which is the portion of the small intestine that is evaluated during colonoscopy. Studies on TI date back a long time when the first description of Crohn's disease (CD) by Burrill Bernard Crohn as a new entity under the name "terminal ileitis" was published in 1932.[1] Crohn's disease primarily involves the terminal ileum though it may affect the entire gastrointestinal (GI) system with focal/patchy, segmental transmural involvement[2] mainly determined by the competency of immune response and genetic predisposition of the affected individual. Terminal ileum is affected in the majority of CD patients,[3] and it may be the only site involved in some, particularly early in the course of the disease.[4,5] For practicing pathologists, the term "TI" has a broader meaning which needs to be further specified since a variety of conditions including ulcerative colitis presenting as backwash ileitis, infections such as *Yersinia enterocolitica*, vasculitis, particularly Behçet's disease, drugs, mainly nonsteroidal anti-inflammatory drugs (NSAIDs), neoplasms, ischemia, and amyloidosis[6,7] may also cause TI.

The assessment of the ileum is part of the complete colonoscopy; however, due to the difficulty in carrying it out, which increases the examination time, and the fact that it does not bring new information for the diagnosis in most cases, its performance in all colonoscopies has been questioned. The data reported in the literature indicates that the detection rate of TI is low, varying from 1%-5% and that ileal examination helped in the diagnosis in 1.0%-7.2% of routine colonoscopies.[8] The efficiency of terminal ileum biopsy evaluation is closely related to adequacy of bowel preparation, endoscopist's skill in accessing terminal ileum through the ileocecal valve during total colonoscopy, correct and accurate sampling of the mucosa regarding the size and number of biopsy pieces, proper orientation, and fixation of the biopsy fragments.[9] Though strongly suggestive, a normal terminal ileal mucosa does not necessarily rule out CD. Normal histology of terminal ileal biopsies may be difficult, particularly for the inexperienced eye due to the presence of Peyer's patches with specialized epithelium together with a physiologically controlled inflammation. Common endoscopy practice of not taking biopsies from the normal-looking terminal ileum further hampers the recognition of normal terminal ileal mucosa by the pathologists. This practice is based upon the data in the literature indicating that biopsies from a normal appearing terminal ileum have

a low diagnostic yield and are not routinely recommended. They are, however of greatest value for patients who undergo endoscopy for known or strongly suspected CD and may show "microscopic TI."[10] Since the progression of the histological findings that are compatible with the diagnosis of CD is largely dependent of disease activity and time, initial onset and later/treated stages of the disease show different microscopic features and different inflammation patterns.

Using a systematic approach to terminal ileal biopsies in order to document all the changes that would aid in the diagnosis and follow-up, we evaluated 2 groups of terminal ileal biopsies taken from patients with a diagnosis of CD. The first group comprised initial biopsies (IB), while the second group included follow-up (control) biopsies from patients under treatment. The aim of this study was, therefore, to define histopathologic features of TI in detail in a cohort of CD patients in an attempt to provide useful information for practicing pathologists.

MATERIALS AND METHODS

A total of 152 terminal ileum biopsies taken from 152 patients with a diagnosis of CD were included in this retrospective study. Terminal ileitis was observed in all 152 patients, 75 with IB and 77 patients with control biopsies (CB) during treatment. Hematoxylin and eosin staining slides were reevaluated by 2 GI pathologists (A.E., B.K.) who were blind to the time of the biopsy. The relevant clinical data including symptoms of fever, abdominal pain, weight loss, perianal disease, presence of fistula, and use of NSAIDs or other drugs, endoscopic and laboratory data including anti-neutrophil cytoplasmic antibody (ANCA) and anti-*Saccharomyces cerevisiae* antibody (ASCA), hemoglobin, leukocyte and thrombocyte counts, CRP, and sedimentation rate were obtained from the electronic medical records of the patients. Patients in CB group were receiving medical treatment primarily with mesalazine (n=53, 68.8%), while infliximab (n=7, 9.1%), adalimumab (n=7, 9.1%), sertolizumab (n=2, 2.6%), steroid (n=2, 2.6%), and azathioprine (n=5, 6.5%) were used as combinations. Apheresis treatment was applied in 1 patient (1.3%). Those with IB did not receive any medication before the biopsy.

Histopathological features of activity (erosion, ulcer, regenerative epithelium, cryptitis, crypt abscess, neutrophils in lamina propria) and chronicity (eosinophils and mononuclear inflammatory cells in lamina propria, crypt distortion, basal lymphoplasmacytosis, fibromuscular obliteration of the villi, shortening/broadening of villi, increased goblet cells in the epithelium—hypercrinia, presence of epithelial metaplasias including pyloric and foveolar metaplasia and Paneth cell hyperplasia, thickening of muscularis mucosa) as previously defined were evaluated for each case. Pattern of lamina propria inflammation as diffuse or patchy/focal and inflammatory cell density in lamina propria as absent/low/high, presence of intraepithelial lymphocytosis, lymphatic dilation, and edema were also noted.

MAIN POINTS

- We emphasize the importance of terminal ileum biopsy in Crohn's disease.
- We reveal histopathological features of chronicity and activity in Crohn's disease.
- We compare inflammatory patterns of terminal ileal mucosa before and after the treatment.

All biopsies were classified into 3 categories for the inflammatory pattern of TI as active/acute ileitis (AI), chronic active (CA), and chronic inactive (CI) based on the extent of the above features of activity and chronicity. Those demonstrating solely features of activity were grouped as AI whereas those presenting features of both activity and chronicity were classified as CA and cases showing only features of chronicity and lacking findings of activity were grouped as CI.

Histopathologic diagnosis of colonic biopsies were retrieved from pathology reports for each biopsy site including terminal ileum, cecum, ascending colon, transvers colon, descending colon, sigmoid colon, and rectum. Involvement patterns were grouped in 3 subtypes depending on the site of inflammatory pathology: isolated TI when only terminal ileum was involved; segmental colitis (SC) when terminal ileum and parts of the colon were involved; diffuse colitis (DC) when terminal ileum was involved with the entire colon.

Informed consent was obtained from all of the patients included in the study. Ethics committee approval was obtained from Ethics Committee of Ankara University Medical School Divison of Surgical Sciences Department of Pathology (Approval number: 2020/14, Date: July 3, 2020). The study was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences software 23.0 for Windows program (IBM; Armonk, NY, USA). Fisher's exact test and Pearson's chi-squared test were used for statistical differences between groups and to determine correlations, respectively. A P-value $\leq .05$ was considered statistically significant.

RESULTS

Patients

Of the 152 cases, 64 (42.1%) were female with a mean age of 43.94 years and 88 (57.9%) were male with a mean age of 37.97 years. The mean age was 40.25 ± 1.81 years for IB group, 40.70 ± 1.86 years for CB groups. The majority of patients (n=129, 84.9%) including all IB groups underwent ileocolonoscopy with multiple colonic biopsies in addition to terminal ileum biopsies except for 23 (15.1%) patients in the CB group who had only terminal ileum biopsies. When the symptoms were evaluated, abdominal pain (84% and 79.2), weight loss (30.7% and 26%), fever (8% and 22.1%), fistula complaints (4% and 15.6%), and perianal disease (5.3% and 13) were the major complaints for IB and CB groups, respectively. Laboratory parameters were as follows for IB group and CB group, respectively: hemoglobin: 13.29 ± 0.24 g/dL, 13.38 ± 0.21 g/dL, leukocyte count: 7.58 ± 0.27, 9.01 ± 1 K/μL, platelet count: 307.36 ± 10.43 K/μL, 310.79 ± 12.03 K/μL, CRP: 14.57 ± 3.6, 13.17 ± 1.91, and sedimentation rate: 18.62 ± 1.87 m/h, 24.29 ± 2.7 m/h.

When the IB and CB groups were compared in terms of demographic features, clinical symptoms and laboratory data, ASCA positivity ($P <$ .001), recurrent fever ($P=.015$), and the presence of fistula ($P=.017$) were significantly higher in CB group compared to IB group. Upper GI endoscopy was performed in 119 (78.3%) patients and revealed reflux esophagitis in 2 patients (1.3%) while 2 cases (1.3%) showed peptic duodenitis, and 8 (5.3%) had focal intraepithelial lymphocytosis in their duodenal biopsies. Helicobacter pylori gastritis was detected in 38 patients (25%). The remaining 69 patients (45.4%) did not have a significant pathology in upper GI.

Table 1. Demographic, Clinical, Endoscopic, and Laboratory Findings

	IB		CB		
Clinicopathologic Parameters	**n**	**%**	**n**	**%**	***P***
Gender					.426
Male	41	54.7	47	61	
Female	34	45.3	30	39	
Antibody situation					
ANCA	5/51	9.8	5/66	7.6	.745
ASCA	9/38	23.7	36/62	58.1	.001
Abdominal pain	63	84	61	79.2	.447
Recurrent fever	6	8	17	22.1	.015
Perianal disease	4	5.3	10	13	.103
Fistula	3	4	12	15.6	.017
Weight loss	23	30.7	20	26	.521
	IB		**CB**		
Clinicopathologic parameters	**Mean**	**SD**	**Mean**	**SD**	***P***
Age (years)	40.25	(±1.81)	40.70	(±1.56)	.803
Number of biopsies	2.8	(±0.16)	2.55	(±0.12)	.400
Hemoglobin	13.29 g/dL	(±0.24)	13.38 g/dL	(±0.21)	.842
Leukocyte count	7.58 K/µL	(±0.27)	9.01 K/µL	(±1)	.399
Thrombocyte count	307.36 K/µL	(±10.43)	310.79 K/µL	(±12.03)	.912
C-reactive protein	14.57	(±3.6)	13.17	(±1.91)	.66
Sedimentation	18.62 m/h	(±1.87)	24.29 m/h	(±2.70)	.174
Defecations/day	3.41	(±0.52)	3.15	(±0.40)	.788

ANCA, antineutrophil cytoplasmic antibody; ASCA, anti-*Saccharomyces cerevisiae* antibody; CB, control biopsies; IB, initial biopsies.

Endoscopy

Endoscopic data revealed that ulcer was the most striking finding in 45 of 66 (68.2%) of IB group while 49 of 68 (72.1%) cases in CB group showed ulceration on endoscopy. Ulcer was detected much less commonly microscopically, unlike endoscopy. It was detected at similar rates in the IB group (26.7%) and the CB group (27.3%) like edema which was observed in 16.7% of IB and 14.7% of CB. Terminal ileum was normal in 10 patients (15.2%) in the IB group and 9 (13.2%) patients in the CB group on endoscopy.

Demographic, clinical, endoscopic, and laboratory data are summarized in Table 1.

Histopathology

Among the features of activity, cryptitis was the most common finding (n=82, 53.9%), followed by ulcer (n=41, 26.9%), erosion (n=28, 18.4%), and crypt abscesses (n=15, 9.8%) in all study cases, while crypt distortion (n=130; 85.5%) was the most common feature of chronicity followed by basal lymphoplasmacytosis (n=100, 65.8% of all cases), villous shortening/broadening (n=90; 59.2%), and fibrosis of lamina propria (n=52; 34.2%). Lamina propria inflammation was focal/patchy in the majority of the cases (n=126; 82.9%) with the remaining showing diffuse lamina propria inflammation (n=26; 17.1%). Epithelial metaplasia were present in terminal ileal biopsies including 42 (27.6%) cases with foveolar metaplasia and 46 (30.2%) with pyloric metaplasia while 50 (32.9%) showed Paneth cell hyperplasia and in 9 cases (5.9%) all 3 were observed. Hypercrinia was observed in 30 (19.7%) cases. While 64 (42.2%) biopsies showed a predominance of neutrophils, 72 (47.4%) demonstrated abundance of mononuclear inflammatory cells, and 87 (57.2%) had predominance of eosinophils in the lamina propria. Lymphoid hyperplasia was seen in 97 cases (63.8%) and non-necrotizing granulomas were detected in only 7 cases (4.6%). Table 2 summarizes the inflammatory features observed in all terminal ileal biopsies.

When IB were compared to CB in terms of histopathological parameters, lymphoid hyperplasia and regeneration were statistically significantly ($P=.002$ and $P=.05$, respectively) higher in IB (n=57, 76%; n=65, 86.7%, respectively) than CB (n=40, 51.9%; n=57, 74%, respectively). Apart from these findings, no significant difference was observed between IB and CB groups for other histopathological features evaluated. Although not statistically significant, when we evaluated IB and CB for presence and types of metaplasia, foveolar metaplasia (n=26, 33.8%) and pyloric metaplasia (n=27, 35.1%) were more frequent in the CB group. Villus shortening (n=51, 66.2%) and crypt distortion (n=69, 89.6%), also features of chronicity, were more common in the CB group. Lamina propria fibrosis (n=28, 36.4%) was more common in the CB group while granulomas (n=4, 5.3% for IB and n=3, 3.9% for CB) and cryptitis (n=39, 52% for IB and n=43, 55.8% for CB) were found at similar rates in both groups. Chronicity and activity features are demonstrated in Figure 1 while comparison of IB and CB for histopathological parameters are summarized in Figure 2 and Table 2.

Table 2. Inflammatory Features in Initial Biopsies and Control Biopsies

	IB (n=75)		CB (n=77)		
	n	**%**	**n**	**%**	***P***
Neutrophils in LP					.082
Low	38	50.7	39	50.6	
High	35	46.7	29	37.7	
Mononuclear cells in LP					.985
Low	39	52	39	50.6	
High	35	46.7	37	48.1	
Eosinophils in LP					.266
Low	36	48	27	35.1	
High	38	50.7	49	63.6	

CB, control biopsies; IB, initial biopsies; LP, lamina propria.

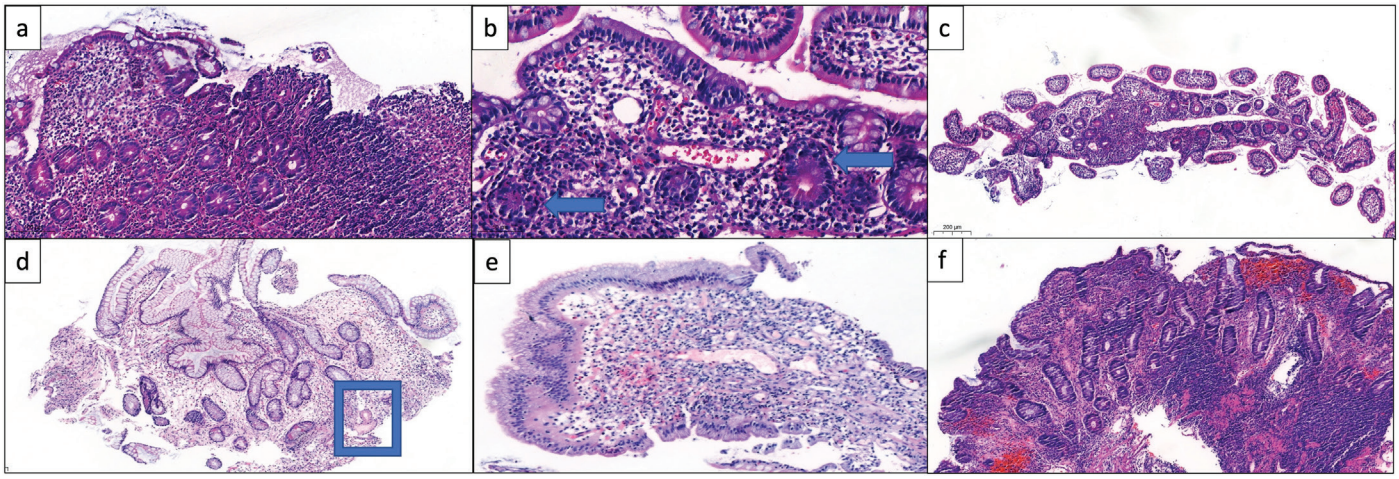

Figure 1. Histologic criteria of activity or chronicity: A. Ulcer. B. Cryptitis (pointed by arrows). C. Focal/patchy involvement. D. Pyloric metaplasia (marked by square). E. Foveolar metaplasia. F. Crypt distortion (hematoxylin and eosin, ×100).

When the TI patterns were evaluated, there were 26 (17.2%) patients classified as AI, whereas CA and CI were equal in number, with 63 (41.4%) patients in each group. The predominant TI pattern was CA in IBs with 32 patients (42.7%), followed by CI with 30 patients (40%), and AI with 13 patients (17.2%), while CB group presented with CI (n=33, 42.9%), followed by CA (n=31, 40.3%) and AI (n=13, 16.9). The TI patterns are summarized in Figure 2.

Depending on the extent of involvement of the colon, for the 129 cases with multiple colonic biopsies, cases were grouped as follows: those presenting with isolated TI, cases with TI and S), and cases with TI and diffuse (pan)colitis (DC). Isolated TI (n=75, 58.1%) was the most common presentation, followed by SC (n=45, 34.9%) and DC (n=9, 7%). In the IB group, the number of patients with TI, SC, and DC was 39 (57.4%), 25 (36.8%), and 4 (5.8%), respectively; the number of patients in the CB group was found to be 36 (59%), 20 (32.8%), and 5 (8.2%) with no significant difference between the groups.

In terms of histopathological features and involvement patterns, pyloric metaplasia showed statistical significance and the likelihood of pyloric metaplasia in SC (7/38, 18.4%) was significantly lower than isolated TI (34/75, 45.3%) or DC (5/9, 55.6%) ($P < .05$). When the association between terminal ileal inflammation patterns and involvement patterns was assessed, in the isolated TI group, CA, CI, and AI patterns were observed in 44 (44.9%), 39 (39.8%), and 15 (15.3%) cases, respectively. In the SC group, CA, CI, and AI groups were found in 15 (33.3%), 21 (46.7%), and 9 (20%) patients, respectively. The 3 patterns were distributed evenly within the DC group; 4 patients (44.4%) showed CA, 3 (33.3%) presented with CI, and 2 (22.2%) had AI, respectively. However, no statistical significance was found in the above correlation analysis. The TI patterns are summarized in Figures 3 and 4.

DISCUSSION

The present study was designed to emphasize the importance of a detailed histopathologic examination of terminal ileal mucosa in CD by evaluating both IB and CB in 2 groups of patients. In the initial biopsy group, more than half of the patients presented with isolated terminal ileum involvement, further confirming the importance of sampling the terminal ileal region for an accurate diagnosis of inflammatory bowel disease, CD, in particular. Interestingly, features of chronicity such as crypt distortion, villous shortening, fibrosis, basal lymphoplasmacytosis, Paneth cell hyperplasia, foveolar, and pyloric metaplasia were

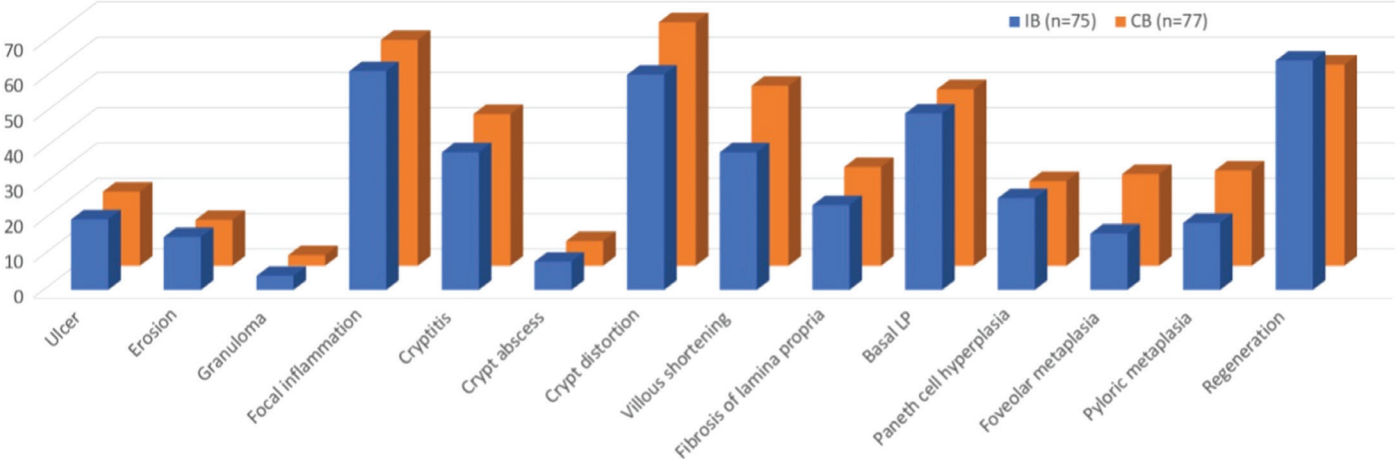

Figure 2. Histopathological features in initial biopsies and control biopsies.

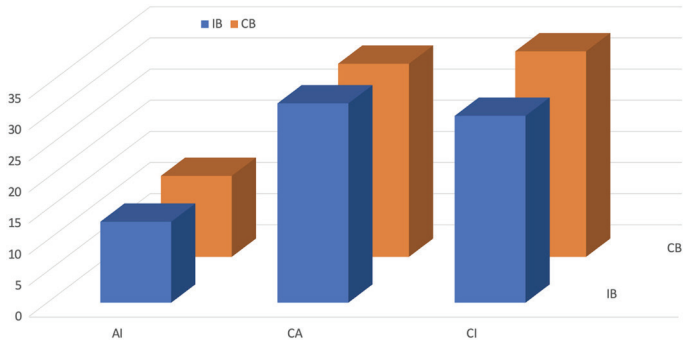

Figure 3. Distribution of inflammation patterns.

detected at a similar rate in both IB and CB groups, suggesting that chronic inflammatory changes dominate the histology of Crohn's TI, regardless of the time of the biopsy.

For pathologists, terminal ileal biopsies are considered precious as terminal ileum is not always sampled during routine colonoscopy due to technical difficulty of sampling this area. The end result for the pathologist is a lack of experience in the interpretation of terminal ileal biopsies, which is further complicated by artifacts caused by inadequate orientation and Peyer's patches obliterating the villi.[11] However, terminal ileal biopsy is particularly important in the diagnostic work-up of CD presenting as isolated ileitis with (not infrequently) normal-looking mucosa on endoscopy.[12] In parallel with this view, the European Crohn's and Colitis Organization recommends ileocolonoscopy as the first line evaluation of CD and taking multiple biopsies from the terminal ileal mucosa.[13,14] Though some investigators argue that taking biopsy from a normal-appearing terminal ileum may not be feasible.[8,15] it is not surprising to find histopathological abnormalities in biopsies even if the terminal ileum appears macroscopically normal in endoscopy, similar to colon. Indeed, the presence of significant histopathological findings in macroscopically normal terminal ileum was reported to be around 5% in the literature.[16,17] In the present study, 15.2% of the IB group and 13.2% of the CB group presented with an endoscopically normal terminal ileum. Though slightly higher than those previously reported in the literature, these results confirm the importance of sampling endoscopically normal-appearing terminal ileal mucosa.

It is important to realize that endoscopic alterations have no specific pathologic features, such as erythema or edema, while some cases of acute or chronic ileitis may not always be evident on endoscopy. Erosion and ulcer are the 2 alterations with the highest disagreement between endoscopists and pathologists,[18] which may result from sampling error during endoscopy. It was stressed in several studies that endoscopic examination when complemented by biopsy was more useful in diagnostic work-up of patients with suspected inflammatory bowel disease.[19,20]

As recommended,[21] taking multiple biopsies from at least 5 different parts of the colon during ileocolonoscopy is equally important in the diagnostic work-up of CD, which characteristically manifests with focal/patchy involvement of the bowel.[10,21] Colonic involvement, reported in around 60% of the cases, may present in a pancolonic or segmental fashion in CD.[22] In the present study 41.9% of cases had colonic involvement in the form of segmental or diffuse (pan)colitis, while nearly half of the patients showed isolated ileitis, emphasizing the importance of performing both ileal and colonic biopsies for the diagnosis of CD.

In inflammatory bowel disease, neutrophilic inflammation is the most prominent feature of histologically active disease[13,23] together with the damage to the surface epithelium characterized by flattening, erosions, and ulcers also reflecting activity of the disease. On the other hand, discontinuous chronic inflammation, focal crypt architectural distortion, and metaplastic epithelia comprise features of chronic disease.[4] In our study, CA ileitis was the most common pattern of inflammation at initial presentation and also during follow-up. Therefore, in line with the literature,[9] architectural findings of chronicity are more suggestive when diagnosing CD in the right clinical context.

In 1 study, of the 17 cases with normal endoscopy and abnormal histopathological changes, significant chronic inflammatory changes were identified in 14 (82.3%). In contrast, 80 cases in which endoscopic abnormalities such as ulcers and erosion were identified in the terminal ileum, 59 (73.8%) also had histologic abnormalities, all but 4 of which were considered by the authors to be those of significant chronic inflammation.[8] These findings indicate the importance of histologic evaluation of terminal ileal biopsy and close collaboration of the endoscopist and the pathologist in the diagnosis of CD.

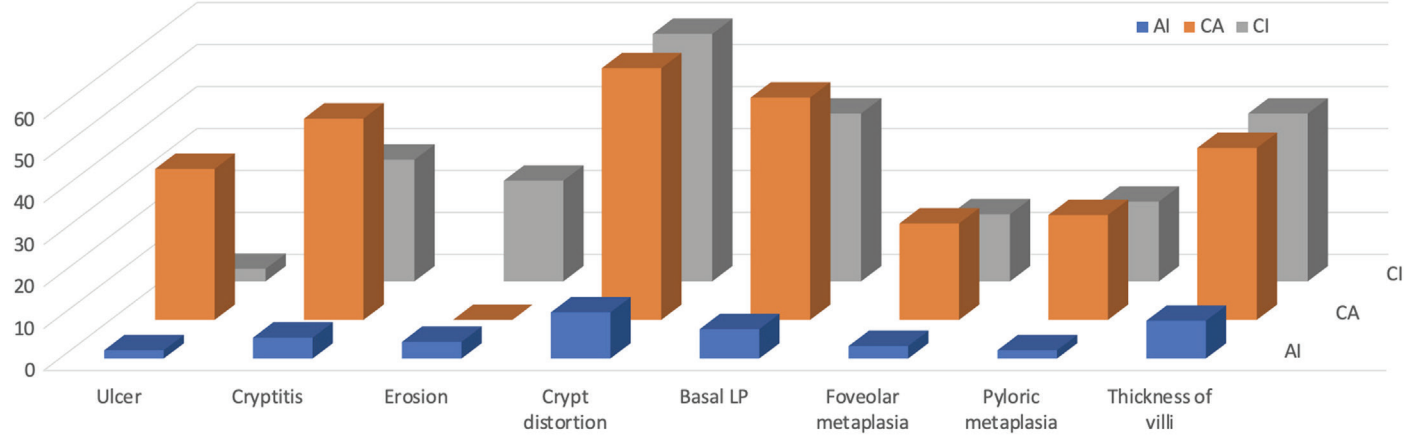

Figure 4. Distribution of histopathological features in relation to inflammatory patterns.

Gastric metaplasia, including pseudopyloric or pyloric gland metaplasia and foveolar metaplasia, is frequently seen in chronic inflammatory conditions, although the underlying mechanism is still not fully understood.[24] While all are encountered in regenerative/reparative states as a reflection of the ulcer-associated cell lineage, pyloric gland metaplasia, in particular, when found, is highly suggestive of CA ileitis of CD.[25,26] On the other hand, Paneth cell metaplasia in the left colon is a frequent finding in ulcerative colitis patients,[27] while it suggests chronicity in colonic CD. Foveolar metaplasia is underdiagnosed and underreported in routine practice, though it is a frequent finding in terminal ileum biopsies from patients with suspected or known CD.[28] Kellermann et al[29] stated that pyloric gland metaplasia may evolve in the course of the disease and is observed in up to 25% of initial ileal biopsies from patients with CD. In the current study, foveolar metaplasia and pyloric metaplasia were observed more frequently in the CB group compared to the IB group. This finding is in accordance with ulcer-associated cell lineage as the underlying mechanism, which requires a longer time corresponding to follow-up biopsies. However, since there was no statistical significance for the difference between the IB and CB groups in terms of these parameters, it is possible to speculate that chronic changes are already settled in CD during the initial period before a diagnostic biopsy is taken.

In a retrospective study of 108 patients presenting as isolated TI with chronic features, 5 (4.6%) developed CD after a median of 32.3 months.[12] whereas another study has shown a progression rate of 14% from isolated CA ileitis to CD.[30] These reports together with our findings, suggest that TI cases with chronic inflammatory features are more likely to progress to CD compared to those without features of chronicity in the terminal ileum. Pure active ileitis, on the other hand, is not a frequent histologic appearance, as features of chronicity seem to develop before endoscopic biopsy is planned possibly due to extended clinical course of the disease.

The ANCA and ASCA which have been used quite frequently in recent years, can predict diagnosis, treatment, and prognosis in inflammatory bowel disease. While ANCA positivity is mainly expected in ulcerative colitis (UC) patients,[31] ASCA positivity is more frequently found in CD patients.[32-34] The fact that ASCA positivity rate was higher than the ANCA positivity rate in our study also supports this. On the other hand, proportionally higher positivity for antibody was found in the CB group than in the IB group. Although a definitive interpretation cannot be made, it can be related to the ANCA evaluation of more patients in the ANCA-positive CB group than in the IB group.

There are some drawbacks of the current study. First, clinical and endoscopic information could not be obtained for all the patients leading to insufficient interpretation of clinicopathological correlations. Because of the evaluation of a biopsy taken from each patient at one time (IB or CB), the time lag between IBs and CBs could not be obtained from patients. Second, but perhaps less importantly, some patients had only terminal ileum biopsies without accompanying colonic biopsies, which allowed additional information regarding the involvement patterns of the disease. Evaluation of inflammatory patterns of Crohn's TI was performed in 2 different set of biopsies from different patient population, which might seem like a weak point of the study. However, we believe that this approach allowed us to assess the inflammatory patterns in treated and untreated patients independently with no additional effect of individual results to mucosal response of the patient. Moreover, evaluation of terminal ileum in these 2 settings together with colonic involvement patterns provided more insight into the biology of the disease. Since we did not focus on the accompanying colitis found in some of the cases, no histologic activity scoring system was used in the study. Inflammatory patterns grouped as active, CA, and CI were determined using similar histopathologic features that are evaluated in such scoring systems. When this is considered from another different point of view, in the other studies, many scoring systems such as inflammatory bowel disease—distribution, chronicity, activity (aka IBD-DCA) are used for this issue.[35] Therefore, although an inflammation scoring such as "low" or "high" is not scientifically sound, we believe that it will affect clinical treatment adequately and effectively, since there is a summary of these parameters in the pathology report given as a result of routine applications. We also hope that, our study design based on the evaluation of both initial and posttreatment CB will help our fellow pathologists to be more confident in the interpretation of terminal ileal biopsies.

CONCLUSION

Terminal ileum is a difficult-to-biopsy region of GI tract making the evaluation of ileal biopsy particularly important. For this reason, a systematic, intertwined histopathological and clinical approach is essential to make an accurate diagnosis. Our results suggest that chronic ileitis characterized by patchy inflammation, either active or inactive, is the predominant inflammation pattern of Crohn's TI, regardless of the time of the biopsy. Though chronicity seems to dominate the histopathological picture of Crohn's TI, both in the initial and in CB taken during follow-up, active ileitis was observed at a similar rate in both groups, emphasizing that disease activity can persist for a long time depending on the treatment modality and patient's response and therefore should be evaluated on a case-by-case basis.

Ethics Committee Approval: Ethics committee approval was obtained from the Ethics Committee of Ankara University Medical School Divison of Surgical Sciences Department of Pathology (Approval number: 2020/14, Date: July 3, 2020).

Informed Consent: Informed consent was obtained from all the patients included in the study.

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