Journal of Clinical and Translational Research 2023; 9(1): 26-32

Journal of Clinical and Translational Research

Journal homepage: http://www.jctres.com/en/home

ORIGINAL ARTICLE

Etiological spectrum of isolated ileo-cecal ulcers in patients with gastrointestinal symptoms

Mayank Bhushan Pateria, Anurag Kumar Tiwari, Vinod Kumar, Dawesh P. Yadav, Sunit Kumar Shukla, Ashutosh Gupta, Gurvachan Singh, Vinod Kumar Dixit*

Department of Gastroenterology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

ARTICLE INFO

Article history:
Received: August 25, 2022
Revised: October 11, 2022
Accepted: November 04, 2022
Published online: December 14, 2022

Keywords:
Ileo-cecal ulcers
Crohn's disease
Intestinal tuberculosis
Colonoscopy

**Corresponding author:*
Vinod Kumar Dixit
Department of Gastroenterology, Institute of Medical Sciences, Banaras Hindu University, Varanasi - 221 005, Uttar Pradesh, India.
Tel: +91-941 520 2449.
E-mail: drvkdixit@gmail.com

© 2022 Author(s). This is an Open-Access article distributed under the terms of the Creative Commons Attribution-Noncommercial License, permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Isolated ileo-cecal region (ICR) ulcers may represent underlying Crohn's disease (CD), intestinal tuberculosis (ITB), bacterial infections (including typhoid), amoebiasis, eosinophilic enteritis, drug-induced sequelae, or neoplasm. Overlapping morphological and microscopic characteristics of many of these diseases make it challenging to unequivocally confirm a diagnosis.
Aims: The aim of the study was to investigate the etiology and clinical outcomes of isolated ileo-cecal ulcers discovered during an ileocolonoscopy in patients with gastrointestinal symptoms.
Methods: Patients with isolated ileo-cecal ulcers and symptoms within the age range of 10 – 80 years were included in the study (N = 100). Patients not giving consent (assent in case of a minor), with a prior diagnosis of tuberculosis or inflammatory bowel disease, with incomplete colonoscopy and associated colonic lesions other than ICR were excluded from the study. Demographics, clinical information, and relevant biochemical and serological tests were recorded. During the colonoscopy, multiple biopsies were taken from the ileo-cecal ulcers for histopathological examination. Repeat ileocolonoscopy was performed as needed in consenting patients.
Results: The mean age and mean duration of symptoms were 36.0 ± 15.6 years and 18.8 ± 21.6 months, respectively. The majority of the patients presented with abdominal pain (59%), followed by diarrhea (47%), weight loss (20%), gastrointestinal bleeding (15%), and fever (11%). A history of taking nonsteroidal anti-inflammatory drugs was present in only 5% of the patients. Mean hemoglobin, C-reactive protein, and albumin levels were 11.6 ± 2.8 g/dL, 6.9 ± 9.5 mg/L, and 3.7 ± 0.8 g/dL, respectively. Based on clinical, colonoscopic, and histopathological findings, initial treatment was symptomatic/antibiotics in 55%, anti-tubercular treatment in 21%, 5-aminosalicylic acid/steroids for CD in 13%, oral budesonide in 10% of patients, and one patient was referred for management of malignancy. Final diagnoses after 8 – 24 weeks of follow-up were non-specific ileitis/colitis (45%), CD (20%), ITB (18%), infective (7%), eosinophilic ileitis/colitis (6%), non-steroidal anti-inflammatory drug-induced (2%), and amoebic and malignant in 1% of patients each.
Conclusions: The majority of patients with ileo-cecal ulcers have specific etiologies. Non-specific ulcers at the ICR can be managed symptomatically; however, close follow-up is necessary as sometimes the ulcers may harbor an underlying specific disease.
Relevance for Patients: Isolated ileo-cecal ulcers are common findings during colonoscopy in both symptomatic and asymptomatic patients. The majority of these ulcers harbor underlying significant diseases that can cause morbidity and mortality if left undiagnosed and untreated. Reaching a specific diagnosis in such cases is not straightforward, and patients are often subjected to repeat examinations.

1. Introduction

The ileo-cecal region (ICR) consists of the distal most part of ileum, ileo-cecal (IC) valve, cecum, and appendiceal orifice [1]. It is common to find abnormalities such as

DOI: http://dx.doi.org/10.18053/jctres.09.202301.003

ulcers located in the ICR during colonoscopy. An ICR ulcer may be defined as a breach and not as simple petechiae or hyperemic lesions in the mucosa in this location. The frequency of such findings is rising with the increasing population, advancing technologies and increased patient awareness and access to healthcare facilities. The ileo-cecal area can be affected in the localized disease process or be a part of the involvement of other bowel segments or any systemic disease. The ICR is an area of physiological stasis, increased absorptive area, decreased digestive function and abundant lymphoid tissue and M cells. It is the most common area of the gastrointestinal tract involved in pathological processes [2,3]. The abnormalities of ICR could be detected on imaging or during ileocolonoscopy. These may represent a variety of diseases such as benign or malignant tumors, infections, inflammatory bowel diseases, ischemia and other conditions. However, these abnormalities on imaging or ileocolonoscopy may be spurious findings without any underlying cause. In various studies on bowel wall thickening, a normal ileocolonoscopy has been found in up to one-third of cases [4,5]. Some patients may have nonspecific ileitis on histopathology and endoscopic abnormalities such as mucosal nodularity and ulcers in these patients may be followed without any treatment in the absence of symptoms [6]. Isolated ICR ulcers pose a significant challenge for a diagnosis and cannot be ignored in symptomatic patients. However, studies in this regard are sparse in the literature. One study concluded that more than 50% of isolated ulcers represent underlying specific diseases and in remaining patients repeat evaluation is necessary if symptoms persist [7]. ICR ulcers may be detected incidentally in asymptomatic persons or may present with pain abdomen, gastrointestinal bleeding (GI bleeding), fever, weight loss, diarrhea, and malabsorption. Etiologies of ICR involvement have been discussed and categorized into common, less common and rare causes in a review [8] and some of these etiologies have been described in detail in another review [1]. In the review by Agarwal *et al.* common causes were intestinal tuberculosis (ITB), Crohn's disease (CD), adenocarcinoma, cecal diverticulitis, appendicitis, bacterial ileocolitis—*shigella, salmonella, campylobacter, clostridium difficile, yersinia,* amebiasis and lymphoma. Less common causes were ischemic, *mycobacterium avium complex*, systemic vasculitis, histoplasmosis, *cytomegalovirus*, other tumors (carcinoid, gastrointestinal stromal tumor, metastasis, and lipoma), and typhlitis. Rare causes were eosinophilic gastroenteritis, endometriosis, lipomatosis of IC valve and IgG4-related disease of IC area [8]. In immunocompromised and post-transplant patients, in addition to tuberculosis and *cytomegalovirus* (CMV); enteric bacterial infections, fungal infections (mucormycosis, aspergillosis, and histoplasmosis), ischemic necrosis of cecum, and lymphoma are important differentials [1,8]. Overlapping morphological and microscopic characteristics of these diseases are a significant challenge to reach a specific diagnosis. There are a few studies in India to date to describe the etiologies of isolated terminal ileal and cecal ulcers [7,9].

2. Materials and Methods

2.1. Study population

The present study is a prospective study designed to investigate the etiopathogenesis of isolated IC ulcers in symptomatic patients who underwent ileocolonoscopic examination and presented with one or more of the following symptoms: abdominal pain, unexplained fever, weight loss, overt or occult GI bleeding, altered bowel habits, diarrhea, and partial bowel obstruction. Patients who refused to give consent (assent in case of a minor), patients with a prior diagnosis of tuberculosis or inflammatory bowel disease and patients with incomplete colonoscopy and associated colonic lesions other than in the ICR were excluded from the study (Figure 1). This study was approved by the institutional ethics committee (Approval No. Dean/EC/2737).

2.2. Objectives

The objectives of the present study were to find out etiology, clinical profile and outcome of ileo-cecal ulcers detected on ileocolonoscopies in patients with GI symptoms.

2.3. Evaluation of patients

All the patients falling within the sampling frame were invited to participate in the study at our center, Department of Gastroenterology, Institute of Medical Sciences, Banaras Hindu University, Varanasi. Demographic, clinical and treatment details were recorded. Relevant biochemical (blood counts, liver function, renal function, C-reactive protein [CRP]) and serological tests including celiac and viral serology were done. Ultrasonography (USG) and cross-sectional imaging of the abdomen were performed as needed. Ileocolonoscopy was performed at our center with colonic preparation using a polyethylene glycol electrolyte-based solution. The procedure was performed under conscious sedation. During the colonoscopy, a careful examination was done for the presence of ulcers in the cecum, IC valve and terminal ileum. If an ulcer was found, multiple biopsies were obtained from the lesion for histopathological examination (HPE) and nucleic acid amplification test (NAAT) for *Mycobacterium tuberculosis* (MTB) complex. Repeat ileocolonoscopy was performed after 8 – 24 weeks in patients who had no improvement in symptoms and gave consent for the same.

2.4. Statistical analysis

In the present study, multiple statistical tools and techniques were applied to investigate IC ulcers. For data analysis, SPSS software version 22 was used. As appropriate, continuous data were expressed as mean ± SD or median. Categorical variables were expressed as percentages. Chi-squared test was used to assess clinical, colonoscopic, laboratory, and histological features to evaluate the presence of any pattern. Intergroup analysis was done using the ANOVA test of statistical significance. $P < 0.05$ is considered to be statistically significant.

DOI: http://dx.doi.org/10.18053/jctres.09.202301.003

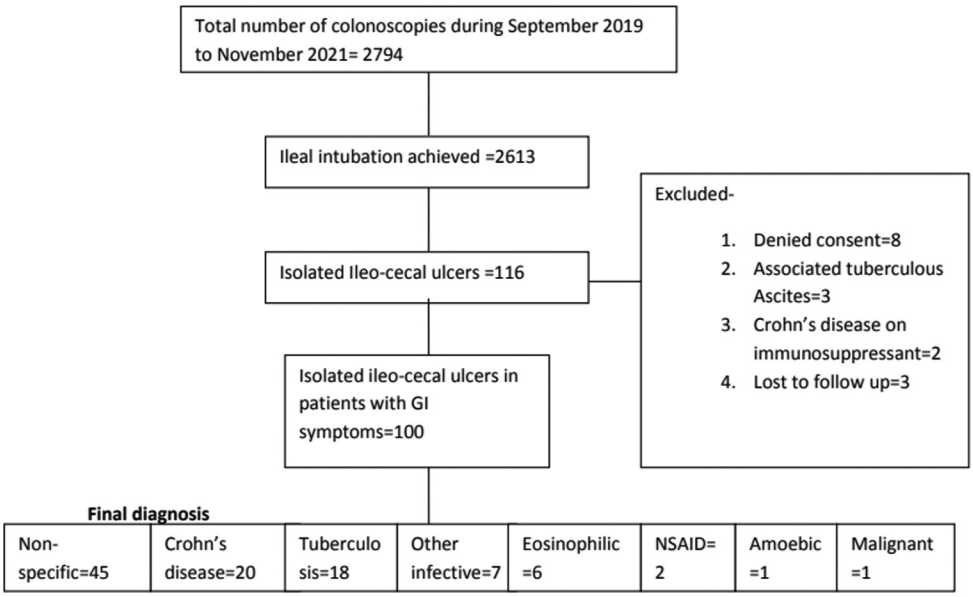

Figure 1. Patient flow chart.

3. Results

From September 2019 to November 2021, 2794 colonoscopies were performed and ileal intubation could be achieved in 2613 patients. Of these, 100 patients (69 males and 31 females) with isolated ICR ulcers were finally included in the study (Figure 1). The mean age of patients was 36 ± 15.7 years (range 10 – 80 years) and the mean duration of symptoms was 18.8 ± 21.6 months. Most common symptoms were abdominal pain (59%), diarrhea (47%), weight loss (20%), GI bleeding (15%), and fever (11%). A history of taking non-steroidal anti-inflammatory drugs (NSAIDs) was present in only 5% of patients. Pallor was present in 18% of patients and right iliac fossa tenderness/lump was present in only half of these pale patients. Clinical examinations of the remaining 82 patients were unremarkable. Mean hemoglobin was 11.6 ± 2.8 (range 3.8 – 16.7 g/dL), mean CRP was 6.9 ± 9.5 (range 3.0 – 55.0 mg/L), and mean albumin level was 3.7 ± 0.7 (range 1.9 – 5.3 g/dL).

Out of 100 patients, 40 were examined with USG abdomen, which demonstrated ICR abnormalities (thickening/mass/lymph nodes) in 23 patients (57.5%). Computed tomography (CT) was done in 32 patients with positive ICR abnormalities in 27 (84.3%) patients. Combined USG and CT were available in 14 patients, with abnormal ICR in 12 (85.7%) patients. In addition to IC ulcers, other abnormalities during colonoscopy were terminal ileal mucosal nodularity (23%), cobble-stoning of mucosa (8%), aphthous ulcers (3%), and mucosal fissuring (11%).

HPE findings included lymphoplasmacytic (LP) mixed infiltrates, architectural distortion, cryptitis/crypt abscess, eosinophilic/neutrophilic infiltrates, goblet cell mucin depletion and granuloma in 93%, 28%, 26%, 25%, 21%, and 15% of patients, respectively. MTB NAAT (Gene Xpert) was positive in 6% and mycobacteria growth indicator tube (MGIT) culture in 3% only. One patient each had nuclear atypia and flask-shaped ulcers in histology, suggesting a diagnosis of malignancy, and amoebic colitis, respectively. Based on clinical, colonoscopic and histopathological findings, initial treatment was symptomatic/antibiotics in 55%, anti-tubercular treatment (ATT) in 21%, 5-aminosalicylic acid (5-ASA)/steroid for CD in 13%, oral budesonide in 10% of patients, and one patient was referred for the management of malignancy.

Repeated colonoscopy was done in 32 patients after 8 – 24 weeks of initial treatment whose symptoms had not resolved significantly. Twenty-five patients had improvement in endoscopic lesions and were continued on initial treatment as required. Seven patients (4 were receiving budesonide and 3 were ATT) had either similar or worsened endoscopic findings compared to the previous one and were subjected to repeat biopsy and histopathology, which suggested a diagnosis of CD. These patients were switched to steroid/5-ASA.

Final diagnoses in all 100 patients were non-specific ileitis/colitis (45%), CD (20%), ITB (18%), infective (7%), eosinophilic ileitis/colitis (6%), NSAIDs induced (2%), and amoebic and malignant (1% each). Based on the final diagnosis, we divided patients into 5 broad groups, namely: non-specific, ITB, CD, eosinophilic and infective groups. Symptom frequency was analyzed retrospectively in these 5 groups and is presented in Table 1. The colonoscopic characteristics of ulcers such as number, location, shape, and IC valve involvement significantly differentiated between the final diagnosis groups ($P < 0.05$). HPE findings like architectural distortion, LP mixed infiltrate, goblet cell mucin depletion, cryptitis/crypt abscess, eosinophils, granuloma, MTB GeneXpert and MGIT culture significantly differentiated between final diagnosis groups ($P < 0.001$).

3.1. Sub-group analysis of non-specific ileitis/ITB/CD

Intergroup analysis was done in the non-specific, ITB and CD groups, using the ANOVA test of statistical significance. Sex,

DOI: http://dx.doi.org/10.18053/jctres.09.202301.003

Table 1. Clinical, biochemical, endoscopic, and histological parameters of all patients

Total (100%)	Non-specific (45%)	Crohn's disease (20%)	Tuberculosis (18%)	Infective (7%)	Eosinophilic (6%)	NSAID (2%)	Amoebic (1%)	Malignant (1%)	*P*-value
Age (years), mean (SD)	33.0 (12.8)	31.9 (12.6)	39.2 (17.8)	45.2 (18.6)	41.3 (20.1)	61 (4)	25 (-)	65 (-)	
Sex (male)	66.7%	75%	72.2%	85.7%	66.7%	50%	100%	100%	
Duration of symptoms (months), mean (SD)	23.3 (23.5)	18.6 (16.0)	19.2 (25.8)	2.0 (2.5)	14.5 (10.0)	57(51)	12	2	0.77
Abdominal pain, %	53	75	66.7	42.9	33.3	50	100	100	0.22
Weight loss, %	13.3	40	33.3	0	0	0	0	0	0.04
Bleeding, %	6.7	5	5.6	100	16.7	100	0	0	0.96
Fever, %	8.9	0	27.8	14.3	0	0	0	100	0.019
Diarrhea, %	26.7	70	55.6	85.7	50	100	0	0	0.003
Hemoglobin, mean (SD)a	13.1 (2.7)	11.3 (2.0)	10.6 (1.9)	6.9 (1.2)	11.9 (2.3)	8.9 (0.3)	10.2 (-)	9.3 (-)	<0.001
CRP, mean (SD)b	3.5 (6.97)	10.6 (7.8)	15.0 (14.2)	4.0 (2.3)	1.0 (0.5)	1.8 (0.3)	2.2 (-)	6.3 (-)	<0.001
Albumin, mean (SD)c	4.2 (0.62)	3.4 (0.7)	3.3 (0.5)	3.2 (0.7)	4.2 (0.3)	3.2 (0.05)	4.1 (-)	2.2 (-)	<0.001
No. of ulcer, %									0.016
Single	20	0	16.7	28.6	0	0	100	100	
Multiple	80	100	83.3	71.4	100	100	0	0	
Location, %									<0.001
Terminal ileum	91.1	50.0	38.9	28.6	66.7	100	0.0	0.0	
Ileo-cecal	2.2	45.0	27.8	14.3	16.7	0.0	0.0	0.0	
Cecal IC valve	6.7	5.0	33.3	57.1	16.7	0.0	100	100	
Gross feature, %									<0.001
Superficial	97.8	35.0	16.7	57.1	100	100	0.0	0.0	
Deep	2.2	65.0	83.3	42.9	0.0	0.0	100	100	
Shape, %									<0.001
Small	80.0	30.0	11.1	14.3	83.3	100	0.0	0.0	
Large	6.7	55.0	77.8	57.1	16.7	0.0	100	100	
Aphthous	6.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Erosions	6.7	5.0	5.6	0.0	0.0	0.0	0.0	0.0	
Irregular	0.0	10.0	5.6	28.6	0.0	0.0	0.0	0.0	
IC valve, %									<0.001
Normal	97.8	50.0	38.9	85.7	100	100	100	0.0	
Deformed	2.2	50.0	61.1	14.3	0.0	0.0	0.0	100	
HPE, %									
Architectural distortion	4.4	95.0	27.8	0.0	0.0	50.0	0.0	100	<0.001
Lymphoplasmacytic infiltrates	97.8	95.0	100	28.6	100	100	100	100	<0.001
Goblet cell mucin depletion	0.0	95.0	11.1	0.0	0.0	0.0	0.0	0.0	<0.001
Cryptitis and crypt abscess	4.4	45.0	44.4	85.7	0.0	0.0	100	0.0	<0.001
Eosinophils	2.2	40.0	27.8	57.1	100	0.0	100	0.0	<0.001
Granuloma	0.0	15.0	61.1	0.0	0	0.0	0.0	0.0	<0.001
Gene Xpert	0.0	0.0	33.3	0.0	0	0.0	0.0	0.0	<0.001
MGIT culture	0.0	0.0	16.6	0.0	0.0	0.0	0.0	0.0	<0.001

[a]Normal value: 11.5 – 16.5 g/dL.[b]Normal value: 0.0 – 6.0 mg/L.[c]Normal value: 3.5 – 5.5 g/dL. NSAID: Non-steroidal anti-inflammatory drugs, CRP: C-reactive protein, IC: Ileo-cecal, HPE: Histopathological examination

abdominal pain, weight loss, bleeding, fever, and diarrhea were compared. Out of these, only weight loss, fever, and diarrhea were significantly associated with these three final diagnoses ($P = 0.040$, $P = 0.019$, and $P = 0.003$, respectively). The mean age and mean duration of symptoms were comparable between the three groups. The mean hemoglobin was significantly higher in the non-specific group as compared to ITB ($P = 0.001$) and CD ($P = 0.022$) and comparable in ITB and CD groups ($P = 1.000$). The mean CRP level was significantly higher in ITB group as compared to the non-specific ($P < 0.001$) and comparable in the ITB and CD groups ($P = 0.471$). The mean albumin level was significantly lower in ITB ($P < 0.001$) and CD ($P < 0.001$) groups compared to non-specific group and comparable between ITB and CD groups ($P = 1.000$). In this study, gross features such

DOI: http://dx.doi.org/10.18053/jctres.09.202301.003

as ulcer location and shape significantly differentiated the non-specific group from ITB and CD ($P < 0.001$) and the number of ulcers was similar in all three groups ($P = 0.102$). Architectural distortion and goblet cell mucin depletion were significantly associated with CD ($P < 0.001$). Presence of a granuloma and positive MTB NAAT/MGIT culture favored a diagnosis of ITB ($P < 0.001$).

4. Discussion

Studies suggest that most common etiology of isolated ulcers in the ICR is *non-specific,* followed by CD, tuberculosis, infective and malignant disorders, among others [7,9]. Primary diagnosis of isolated ICR ulcers is confirmatory in a subset of patients where we find specific histopathological/microbiological evidence for tuberculosis (Tubercular Bacilli, positive deoxyribonucleic acid polymerase chain reaction [DNA PCR], caseating granuloma, etc.), malignancy and *E. histolytica* (trophozoites and/or flask-shaped ulcers in biopsy), etc. In most patients, a biopsy is not confirmatory and a constellation of clinical, biochemical, serological, endoscopic and histological findings is required to reach a diagnosis. Furthermore, the treatment trial failure for the primary diagnosis necessitates further examination and/or a change in treatment for alternate diagnoses. In our study, we took a similar approach in describing various ICR ulcers. Statistical findings of subgroup analyses comparing nonspecific, CD and ITB can be taken for hypothesis generation only as the groups were small in the present study.

Final diagnoses in all 100 patients were non-specific ileitis (45%), CD (20%), ITB (18%), infective (7%), eosinophilic ileitis/colitis (6%), NSAIDs induced (2%), and amoebic and malignant in 1% each. These frequencies are consistent with earlier reports [7,9,10] where non-specific ulcers were most common followed by CD or ITB. Patients with non-specific ileitis are at risk of developing overt CD in future [11]. However, the risk is low (5.4%) and watchful waiting would be a reasonable strategy [12].

The mean age and duration of symptom onset to diagnosis were similar across the non-specific, ITB and CD groups. Most of the patients presented with abdominal pain (59%), followed by diarrhea (47%), weight loss (20%), GI bleeding (15%), and fever (11%). These findings are consistent with other studies [7,9]. However, in the study by Mehta *et al.* diarrhea was predominant symptom (77%), followed by abdominal pain (59%) [7]. A comparison between the non-specific, CD, and ITB groups concluded that the presence of diarrhea, weight loss, fever, lower hemoglobin, high CRP, and low albumin were significantly associated with CD/ITB versus the non-specific group. These findings are consistent with a previous study by *Kedia et al*. [6]

In the present study, a history of GI bleeding was present in all patients with a final diagnosis of "infective" and "NSAID induced" ulcers. However, the frequencies of GI bleeding were comparable in non-specific, ITB, and CD groups.

In the present study, abnormal findings on imaging were 57% on the USG abdomen, 84% on the CT abdomen and 85% when both CT and USG were combined. In one study, Kumar *et al.* concluded that the majority of patients with IC wall thickening on CT had an underlying disease and should be further investigated by ileocolonoscopy and biopsy. In their cohort of 50 patients, the most common diagnosis was tuberculosis (48%), followed by CD (20%) [13]. One study demonstrated the role of combined 2-deoxy-2-fluorine-18-fluoro-D-glucose (^{18}F-FDG)-positron emission tomography and CT enterography (PET-CTE) in the discrimination of clinically significant and insignificant diagnoses and concluded that it may help guide the need for colonoscopy in patients suspected to have ileo-cecal thickening on CT [14].

Colonoscopic findings of isolated superficial and small terminal ileal ulcers with normal IC valve significantly favored non-specific diagnosis over CD and ITB. However, the number of ulcers was similar across all three groups. Endoscopic findings of large ulcers, deep ulcers and deformed IC valve significantly differentiated CD/ITB from the non-specific group in our study.

Tuberculosis, both pulmonary as well as intestinal, is prevalent in India and differentiating intestinal lesions from CD remains a challenge. ITB is a form of extrapulmonary tuberculosis which is paucibacillary and carries a very low yield of direct microbiological or pathological evidence (acid-fast bacilli, NAATs, culture, and caseating granulomas) [15,16]. In a recent meta-analysis, the pooled sensitivity and specificity of Xpert MTB/RIF on intestinal tissue was 23% (95% C.I., 16 – 32%) and 100% (95% C.I., 52 – 100%) [17]. Many reports have been published in this regard, including the usefulness of multi-targeted loop-mediated isothermal amplification (LAMP) and machine learning [18-21]. However, being a resource-poor country, we often depend upon traditional methods like clinical, endoscopic, histopathology, and MTB NAAT/culture. In our study, the finding of isolated LP infiltrates in HPE significantly favored a diagnosis of non-specific ulcers over CD and ITB. The presence of granuloma, positive TB PCR, and positive MGIT culture exclusively favored ITB, while architectural distortion and goblet cell mucin depletion significantly favored the diagnosis of CD over ITB.

Patients with a final diagnosis of eosinophilic enteritis had multiple, small and superficial ulcers located predominantly in the terminal ileum with a normal IC valve. Predominant eosinophilic and neutrophilic infiltrates were the main histopathological findings in these patients. Eosinophilic predominant infiltrates can also be observed in helminthic infections (e.g., pinworms and hookworms), inflammatory bowel disease, autoimmune disease (e.g., scleroderma and Churg–Strauss syndrome), celiac disease, drug reactions and in association with the hypereosinophilic syndrome [22]. However, in the present study, appropriate tests were not performed to individually exclude the possibility of these entities, and hence a few of our cases could represent these diagnoses if investigated further.

The single patient with a diagnosis of amoebic colitis presented with abdominal pain and had a large deep ulcer in the cecum that responded to oral Metronidazole.

DOI: http://dx.doi.org/10.18053/jctres.09.202301.003

The limitations of our study are a short duration of follow-up, limited use of imaging in selected patients and non-utilization of fecal markers for inflammation and enteroscopy.

5. Conclusions

Our study concludes that most patients with ICR ulcers have specific etiologies and therefore require careful evaluation. Imaging, in addition to biochemical and histological parameters, helps reach a specific diagnosis. Repeat colonoscopy and sometimes a change in the initial treatment are useful tools when there is no response. Isolated LP infiltrates in HPE favors non-specific diagnosis over CD and ITB. The presence of granuloma, positive TB PCR and positive MGIT culture in the biopsy sample are diagnostic for ITB, while architectural distortion and goblet cell mucin depletion favor a diagnosis of CD over ITB. Non-specific ulcers at ICR can be managed symptomatically. However, a close follow-up is necessary to detect any significant disease.

Acknowledgments

None.

Funding

The authors would like to acknowledge and extend their appreciation to Institution of Eminence (IoE) Cell, Banaras Hindu University, Varanasi, India, for providing research grant (IoE Scheme no 6031) to Dr. Anurag Kumar Tiwari.

Conflicts of Interest

All authors declare no conflicts of interest.

References

[1] Tang SJ, Wu R. Ilececum: A Comprehensive Review. Can J Gastroenterol Hepatol 2019;2019:1451835.

[2] Horvath KD, Whelan RL. Intestinal Tuberculosis: Return of an Old Disease. Am J Gastroenterol 1998;93:692–6.

[3] Moss JD, Knauer CM. Tuberculous Enteritis. A Report of Three Patients. Gastroenterology 1973;65:959–66.

[4] Iadicola D, De Marco P, Bonventre S, Grutta EM, Barletta G, Licari L, *et al*. Bowel Wall Thickening: Inquire or not Inquire? Our Guidelines. G Chir 2018;39:41-4.

[5] Al-Khowaiter SS, Brahmania M, Kim E, Madden M, Harris A, Yoshida EM, *et al*. Clinical and Endoscopic Significance of Bowel-wall Thickening Reported on Abdominal Computed Tomographies in Symptomatic Patients with no History of Gastrointestinal Disease. Can Assoc Radiol J 2014;65:67-70.

[6] Kedia S, Kurrey L, Mouli VP, Dhingra R, Srivastava S, Pradhan R, *et al*. Frequency, Natural Course and Clinical Significance of Symptomatic Terminal Ileitis. J Dig Dis 2016;17:36-43.

[7] Mehta V, Gupta A, Mahajan R, Narang V, Midha V, Sood N, *et al*. Symptomatic Isolated Terminal Ileal Ulcers: Etiology and Clinical Significance. Endosc Int Open 2017;5:E539-46.

[8] Agarwala R, Singh AK, Shah J, Mandavdhare HS, Sharma V. Ileocecal Thickening: Clinical Approach to a Common Problem. JGH Open 2019;3:456-63.

[9] Toshniwal J, Chawlani R, Thawrani A, Sharma R, Arora A, Kotecha HL, *et al*. All Ileo-cecal Ulcers are not Crohn's: Changing Perspectives of Symptomatic Ileocecal Ulcers. World J Gastrointest Endosc. 2017;9:327-33.

[10] Liu JX, Wang HH. Clinical and Pathological Features of Benign Ileocecal Ulcerative Lesions Discovered by Ileocolonoscopy: Analysis of 31 Cases. Zhonghua Yi Xue Za Zhi 2008;88:823-5.

[11] Smith RL, Taylor KM, Friedman AB, Majeed A, Perera N, Gibson PR. Nonspecific Ileitis: Impact of Histopathology and Gastrointestinal Ultrasound in Achieving the Diagnosis of Crohn's Disease. JGH Open 2022;6:388-94.

[12] Agrawal M, Miranda MB, Walsh S, Narula N, Colombel JF, Ungaro RC. Prevalence and Progression of Incidental Terminal Ileitis on Non-diagnostic Colonoscopy: A Systematic Review and Meta-analysis. J Crohns Colitis 2021;15:1455-63.

[13] Kumar A, Rana SS, Nada R, Kalra N, Sharma RK, Dutta U, *et al*. Significance of Ileal and/or Cecal Wall Thickening on Abdominal Computed Tomography in a Tropical Country. JGH Open 2018;3:46-51.

[14] Singh AK, Kumar R, Gupta P, Kumar MP, Mishra S, Mandavdhare HS, *et al*. FDG-PET-CT Enterography Helps Determine Clinical Significance of Suspected Ileocecal Thickening: A Prospective Study. Dig Dis Sci 2021;66:1620-30.

[15] Kumar S, Bopanna S, Kedia S, Mouli P, Dhingra R, Padhan R, *et al*. Evaluation of Xpert MTB/RIF Assay Performance in the Diagnosis of Abdominal Tuberculosis. Intest Res 2017;15:187-94.

[16] Du J, Ma YY, Xiang H, Li YM. Confluent Granulomas and Ulcers Lined by Epithelioid Histiocytes: New Ideal Method for Differentiation of ITB and CD? A Meta Analysis. PLoS One, 2014;9:e103303.

[17] Sharma V, Soni H, Kumar MP, Dawra S, Mishra S, Mandavdhare HS, *et al*. Diagnostic Accuracy of the Xpert MTB/RIF Assay for Abdominal Tuberculosis: A Systematic Review and Meta-analysis. Expert Rev Anti Infect Ther 2021;19:253-65.

[18] Pulimood AB, Amarapurkar DN, Ghoshal U, Phillip M, Pai CG, Reddy DN, *et al.* Differentiation of Crohn's Disease from Intestinal Tuberculosis in India in 2010. World J Gastroenterol 2011;17:433-43.

[19] Kedia S, Das P, Madhusudhan KS, Dattagupta S, Sharma R, Sahni P, *et al*. Differentiating Crohn's Disease from Intestinal Tuberculosis. World J Gastroenterol 2019;25:418-32.

DOI: http://dx.doi.org/10.18053/jctres.09.202301.003

[20] Sharma M, Sinha SK, Sharma M, Singh AK, Samanta J, Sharma A, *et al*. Challenging Diagnosis of Gastrointestinal Tuberculosis Made Simpler with Multi-targeted Loop-mediated Isothermal Amplification Assay. Eur J Gastroenterol Hepatol 2020;32:971-5.

[21] Weng F, Meng Y, Lu F, Wang Y, Wang W, Xu L, *et al*. Differentiation of Intestinal Tuberculosis and Crohn's Disease through an Explainable Machine Learning Method. Sci Rep 2022;12:1714.

[22] Alfadda AA, Storr MA, Shaffer EA. Eosinophilic Colitis: Epidemiology, Clinical Features, and Current Management. Therap Adv Gastroenterol 2011;4:301-9.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

DOI: http://dx.doi.org/10.18053/jctres.09.202301.003