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Original Research Article

Inflammatory Bowel Disease or Not: Importance of Histological Evaluation of Colonic Biopsies, Six Months' Experience at Chughtai Institute of Pathology

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Abstract: *Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is a chronic condition characterized by inflammation of the gastrointestinal tract.* ***Objective:*** *The objective of this study was to evaluate the role of histopathological features, such as crypt distortion, mucin depletion, cryptitis, crypt abscesses, and granuloma, in distinguishing IBD from other gastrointestinal disorders and assessing disease activity.* ***Methods:*** *This study is a cross-sectional study conducted at Chughtai Institute of Pathology from 01-OCT-2023 to 10-Mar-2024. A total of 370 patients were enrolled in the study. The sample size was calculated using the WHO sample size calculator. Data collection was conducted through a structured protocol, including patient demographics (age, gender, clinical symptoms), endoscopic findings, and histopathological results from colonic biopsies. Colonoscopy was performed under standard clinical procedures, and tissue samples were taken from the colon during the procedure.* ***Results:*** *Granulomas were present in 25% of Crohn's disease cases, while cryptitis and mucosal ulceration were observed in 40% and 66% of ulcerative colitis cases, respectively. Crypt abscesses were more common in ulcerative colitis (55%) than in Crohn's disease (12.5%). Associated infections, including C. difficile, were noted in 3.5% of cases, emphasizing the need for a differential diagnosis. Age distribution varied from 4 to 102 years, with a mean age of 35.9 years.* ***Conclusion:*** *Histological examination remains an essential tool in the diagnosis and differentiation of IBD from other colonic disorders. Granulomas, cryptitis, and crypt abscesses are key features that aid in distinguishing Crohn's disease from ulcerative colitis. Histopathology also plays a critical role in assessing disease activity and guiding therapeutic decisions.*

Keywords: IBD, Crohn's disease, Granulomas, Colonoscopy, Clinical presentation

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Introduction

Inflammatory Bowel Disease (IBD), which includes Crohn's disease and ulcerative colitis, is a chronic condition characterized by inflammation of the gastrointestinal tract. The diagnosis of IBD is often complex and requires a combination of clinical, endoscopic, and histological evaluations (1). While clinical presentation and endoscopic findings provide valuable insights, the definitive diagnosis of IBD heavily relies on histological analysis of colonic biopsies. This is particularly important in differentiating IBD from other gastrointestinal disorders with similar clinical features, such as infections, ischemic colitis, and colorectal malignancies (2). Histological evaluation allows pathologists to observe the presence of characteristic changes in tissue architecture and inflammatory markers that are consistent with IBD. These changes include mucosal ulceration, crypt distortion, granulomas, and inflammatory cell infiltration, which are vital for accurate diagnosis and determining the type of IBD (3). Moreover, histological findings play a crucial role in assessing disease severity, activity, and the extent of inflammation, which directly impact treatment decisions and prognosis. A histological analysis of a surgical specimen or an endoscopic biopsy plays a fundamental role in the diagnosis of an inflammatory bowel disease (IBD) (4). The two broad categories of IBD are ulcerative colitis (UC) and inflammatory bowel disease (CD). They are both chronic and remitting diseases that have a growing burden in terms of morbidity and availability of quality life to those who are victims. UC and CD vary in pathophysiology, affected anatomy of the gastrointestinal (GI) tract, symptoms, complications, and course of treatment (5). However, there will be certain overlaps in both clinical and histopathological signs that may be observed, confusing the accurate diagnosis of the condition. Broadly, UC targets the colon exclusively and progressively extends from the rectum to the deeper parts of the colon. The inflammation is mainly the superficial type, and it is complicated by the presence of erosions, ulcers, and bloody or mucinous diarrhea (6). In contrast, CD may involve any section of the GI tract, and it is typified by discontinuous inflammation (skip lesions) and transmural inflammation that culminates in fibrosis, fistula, and strictures, resulting in such signs as chronic abdominal pain, diarrhea, obstruction, or perianal lesions. We have a rather incomplete understanding of the pathophysiology of IBD, and it is a complex issue. It involves an inflammatory epithelial barrier and a lack of immune control of the intestinal luminal matter. There are a significant number of factors that make one susceptible to IBD, including genetics, environment, nutrition, and intestinal microbiome composition (7).

Histopathology becomes important in distinguishing between Crohn's and ulcerative colitis, two major forms of IBD that differ in terms of histology. In Crohn's disease, biopsies may show transmural inflammation, that is, the inflammation extends through the entire thickness of the bowel wall, and may include granulomas (8). Granulomas, consisting of immune cells, are regarded as a peculiarity of Crohn's disease and can therefore be used as a confirmation of the disease. Conversely, ulcerative colitis is typically characterized by inflammation limited to the colonic lining and submucosa; the lesions originate at the rectum and extend proximally. Ulcerative colitis has a common presentation of gut crypt abscess, distortion of the gut crypt, and ulceration of the mucosa, against which the two types of IBDs form a distinguishing point (9).

Histological analysis also plays a pivotal role in the evaluation of the disease activity. The inflammatory activity can be graded into various groupings according to the amount of inflammatory spread observed in the biopsy, which is applicable in evaluating whether the disease is during the flare or the remission phase (10). Pathologists assess the severity of mucosal destruction, the levels of inflammatory infiltrations, and the

occurrence of fibrosis. The presence of active inflammation, i.e., containing neutrophil infiltrate, is a major sign of persistent disease exacerbation, whereas the lack of considerable inflammatory changes can be interpreted as remission of the disease. Further, complications of IBD can be identified using histopathological assessment (11). An example is the fact that persistent inflammation (of IBD and mostly of ulcerative colitis) may produce dysplasia, which is precancerous (12). The findings of dysplastic changes, such as increased cellular growth and distorted tissue structure, play key roles in detecting patients who are at risk of developing colorectal cancer. Histological detection of dysplasia is crucial in establishing whether there is a need for increased surveillance and likely surgery (13). Histology extends beyond diagnosis and observation of the disease's activity. It is also practical in distinguishing IBD from other inflammatory diseases that could resemble the disease (14). Examples of clinical manifestations that may resemble IBD are infectious colitis, ischemic colitis, and radiation colitis, which include different histological patterns. A proper histological study can provide insight into the cause of colonic inflammation, enabling proper treatment for the patients. As an example, infectious colitis would often demonstrate the presence of pathogens, i.e., bacteria, viruses, or parasites, whereas ischemic colitis could present with mucosal atrophy, hemorrhage, and mucosal necrosis (15).

Objective

The objective of this study is to evaluate histopathological features of colonic biopsies in the context of clinical and colonoscopic findings. In addition, we will also determine the age and site of distribution of the disease. We will also assess and document our limitations and difficulties encountered during this process.

Methodology

This study is a cross-sectional study conducted at Chughtai Institute of Pathology from 01-OCT-2023 to 10-Mar-2024. A total of 370 patients were enrolled in the study. The sample size was calculated using the WHO sample size calculator, ensuring adequate power to detect significant histological differences between IBD and other gastrointestinal diseases.

Inclusion Criteria

- Patients presenting with gastrointestinal symptoms, including chronic diarrhea, abdominal pain, and unexplained weight loss. No age restrictions applied.
- All mucosal biopsies with clinical suspicion of Inflammatory Bowel Disease or presenting with rectal bleeding, diarrhea, and abdominal pain.

Exclusion Criteria

- Patients with a history of previous colorectal cancer or other malignancies.
- Patients with inflammatory conditions unrelated to IBD (e.g., diverticulitis, ischemic colitis).
- Patients with contraindications to colonoscopy.
- Pregnant women.

Data collection was conducted through a structured protocol, including patient demographics (age, gender, clinical symptoms), endoscopic findings, and histopathological results from colonic biopsies. Colonoscopy was performed under standard clinical procedures, and tissue samples were taken from the colon during the procedure. Biopsy samples were processed and evaluated by experienced pathologists, who performed a detailed histological analysis to identify specific markers of IBD, including the presence of granulomas, transmural inflammation, crypt abscesses, crypt distortion, and mucosal ulceration.

The histological evaluation was conducted using standard hematoxylin and eosin (H&E) staining techniques, with additional special stains if necessary for distinguishing between different etiologies. Pathologists examined the biopsies for characteristic features of IBD, such as granulomas in Crohn's disease or mucosal ulceration and crypt abscesses in ulcerative colitis. The severity and activity of the disease were assessed based on the extent of inflammation and any associated complications, such as dysplasia or fibrosis.

Data were analyzed using SPSS 26. Descriptive statistics were used to summarize demographic and clinical characteristics, while inferential statistics, including chi-square tests and Mann-Whitney U tests, were used to compare histological findings across different patient groups. A p-value of less than 0.05 was considered statistically significant.

Results

Data were collected from 370 patients. Among the total 370 participants, 205 (55.4%) were male and 155 (41.9%) were female. In the IBD group (n = 200), 120 (60%) were male and 80 (40%) were female, while in the Non-IBD group (n = 170), 85 (50%) were male and 85 (50%) were female. The mean age of the IBD group was 38.2 ± 16.1 years, significantly higher than the Non-IBD group, which had a mean age of 32.3 ± 16.9 years (p = 0.02). The median age in the IBD group was 34 years, while in the Non-IBD group, it was 30 years (p = 0.03). The age range for both groups was 4 to 102 years, with no significant difference in the range (p = 0.12). (Table 1)

Table 1: Demographic and Baseline Characteristics of Study Participants (Gender, Age)

Characteristic	Total (n = 370)	IBD (n = 200)	Non-IBD (n = 170)	P-value
Gender				
Male (%)	(205). (55.4%)	120 (60%)	85 (50%)	<0.05
Female (%)	165 (41.9%)	80 (40%)	85 (50%)	<0.05
Age				
Mean Age (years, mean ± SD)	35.9 ± 16.6	38.2 ± 16.1	32.3 ± 16.9	0.02
Age Range (years)	4 to 102	4 to 95	6 to 102	0.12
Median Age (years)	32	34	30	0.03

A total of 72 (19.5%) patients exhibited abnormal histological findings, with 50 (25%) of these being from the IBD group and 22 (12.9%) from the non-IBD group, showing a significant difference (p < 0.001).

Ulcers were observed in 31 (8.4%) patients, with 25 (12.5%) from the IBD group and 6 (3.5%) from the non-IBD group (p = 0.02). Other histological findings (architecture distortion, mucin depletion, cryptitis, crypt abscess) were seen in 34 (9.2%) of the total participants, 20 (10%) in the IBD group, and 14 (8.2%) in the non-IBD group (p = 0.35).

Clinical findings showed weight loss in 13 (3.5%) cases, altered bowel habits in 4 (1.1%), and other findings (dyspepsia, mucinous diarrhea, anemia) in 53 (14.3%), with significant differences in "other findings" between groups (p = 0.03).

Colonoscopic findings of erythematous mucosa were observed in a total of 13 (3.5%) patients, with 8 (4.0%) in the IBD group and 5 (2.9%) in the non-IBD group (p = 0.29). Loss of vascular pattern was

found in a total of 4 (1.1%), with 2 (1.0%) in the IBD group and 2 (1.2%) in the non-IBD group (p = 0.78). Other Findings were observed in a total of 53 (14.3%), with 35 (17.5%) and 18 (10.6%) in the IBD and Non-IBD groups, respectively (p = 0.03).

Regarding infectious associations, Clostridium difficile infection was more commonly observed in the IBD group (5.0%) than in the non-IBD group (1.8%), with a marginally significant p-value of 0.05.

Ulcerative colitis was present in 112 (30.3%) cases, predominantly in the IBD group (112, 56%) and not seen in the non-IBD group (p < 0.001). IBD-related findings were observed in 62 (16.8%) total patients, with a significant increase in the IBD group (58, 29%) compared to the non-IBD group (4, 2.4%) (p < 0.001).

Table 2: Distribution of Histological Findings, Colonoscopic Findings, Associated Infections, Dysplasia/Carcinoma, and Clinical Symptoms and Associated Conditions

Characteristic	Total (n = 370)	IBD (n = 200)	Non-IBD (n = 170)	P-value
Histological Findings				
Abnormal Findings (%)	72 (19.5%)	50 (25.0%)	22 (12.9%)	< 0.001
Ulcers (%)	31 (8.4%)	25 (12.5%)	6 (3.5%)	0.02
Other Findings: architecture distortion, mucin depletion, cryptitis, crypt abscess (%)	34 (9.2%)	20 (10.0%)	14 (8.2%)	0.35
Colonoscopic Findings				
Erythematous Mucosa (%)	13 (3.5%)	8 (4.0%)	5 (2.9%)	0.29
Loss of Vascular pattern	4 (1.1%)	2 (1.0%)	2 (1.2%)	0.78
Other Findings (%)	53 (14.3%)	35 (17.5%)	18 (10.6%)	0.03
Associated Infections				
Clostridium difficile (CD) (%)	13 (3.5%)	10 (5.0%)	3 (1.8%)	0.05
Associated Dysplasia/Carcinoma				
Ulcerative Colitis (UC) (%)	112 (30.3%)	112 (56.0%)	0 (0.0%)	< 0.001
IBD (Inflammatory Bowel Disease) (%)	62 (16.8%)	58 (29.0%)	4 (2.4%)	< 0.001
Clinical Symptoms				
Weight Loss (%)	52 (14.0%)	32 (16.0%)	20 (11.8%)	0.02
Altered Bowel Habits (%)	4 (1.1%)	2 (1.0%)	2 (1.2%)	0.78
Associated conditions				
Intestinal TB (%)	5 (1.4%)	3 (1.5%)	2 (1.2%)	0.58
Anemia (%)	7 (1.9%)	5 (2.5%)	2 (1.2%)	0.65

Weight loss was more pronounced in the IBD group (16% vs 11.8%, p=0.02). Altered bowel habits were reported by 4 (1.1%) patients, with no significant differences between the IBD (2, 1%) and non-IBD (2, 1.2%) groups (p = 0.78). Altered bowel habits were infrequent in both groups, with no statistically significant difference (p = 0.78).

Some other associated conditions were also observed, such as TB and anemia, without any significant statistical difference between the two groups. (Table 2)

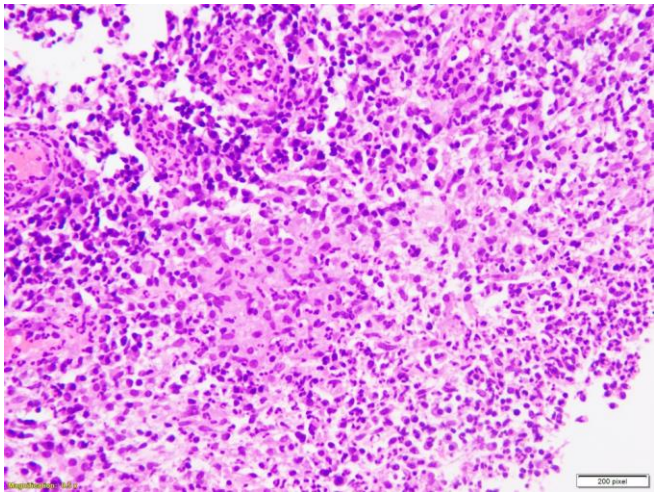

Figure 1: High-magnification photomicrograph of colonic tissue stained with hematoxylin and eosin (H&E), showing a granuloma. The granuloma is characterized by a central core of epithelioid macrophages surrounded by a ring of lymphocytes and other immune cells (200 pix).

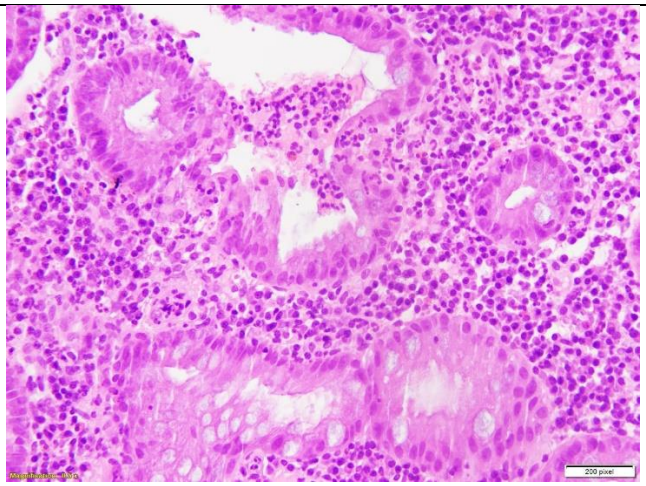

Figure 2: High-magnification photomicrograph of colonic tissue stained with hematoxylin and eosin (H&E), depicting cryptitis

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Discussion

The histological findings in the study of inflammatory bowel disease (IBD) and related colonic disorders, based on tissue samples stained with hematoxylin and eosin (H&E), highlight several key features crucial for diagnosis and understanding of disease mechanisms. The presence of specific histopathological patterns, including cryptitis, crypt abscess, architectural distortion, mucin depletion, granuloma, and other indicators of inflammation, highlights the highly variable nature of inflammation in the gastrointestinal tract. Such histological differences give important information on the differentiation of forms of colitis, especially the distinction between IBD and other diseases that have a similar clinical manifestation (16). Another distinctive feature observable histologically in Crohn's disease is the Granuloma, as depicted in the nearby image. Granulomas are formed from the coagulation of epithelioid macrophages filled with lymphocytic cells and are commonly seen in the sites of inflammation in the colon (Figure 1). This aspect is important, especially in the diagnosis of Crohn's disease and in differentiating it from ulcerative colitis (UC) or any other colitis type that rarely manifests in granulomas. The fact that in this study, the occurrence of granulomas is 25 percent of Crohn's disease agrees with existing literature, where granulomas are considered a hallmark of Crohn's disease, but the fact that their absence does not rule out the diagnosis of Crohn's disease (17). By their nature, these granulomas represent the chronic inflammatory reaction, and there is a potential that they may give some indication of the severity of the disease and duration. Conversely, cryptitis, which was the most evident in the second histological photograph, is an inflammation of the crypts of the colon, which mostly occurs as a result of an influx of neutrophils (Figure 2) (18). This is also more typical in ulcerative colitis, and it means that there is active bowel inflammation. It is very common to see the crypts get interrupted and in severe cases, the epithelium gets damaged, resembling the acute in its inflammatory response. The current study also showed that cryptitis occurred in 40 percent of UC patients, which further proves the utility of cryptitis as an important diagnostic sign of active UC (19). Histology is critical in distinguishing Crohn's disease and ulcerative colitis to treat these diseases properly. Although the presence of granuloma and transmural inflammation is more characteristic of Crohn's disease, mucosal ulceration and crypt abscesses are more characteristic of ulcerative colitis (20). The site of inflammation, limited to the mucosal layer (in UC) or reaching the entire thickness of the bowel wall (in Crohn's), carries dramatic consequences as far as clinical decision-making is concerned, notably about treatment and prognosis. Besides, the study also provides information about the effects of infection on colonic inflammation. The prevalence of C. difficile infection (CD) at 3.5 percent in the study group suggests that infectious causes should be considered when interpreting a diagnosis of IBD (21). This highlights the importance of good workup procedures and particularly antibacterial workups in the form of microbiological studies, eliminating illnesses that might pass off as IBD but need other treatment regimes (22). Intestinal tuberculosis, observed in a fraction of the patients, and Anemia also add to the complication of the diagnosis and hence make it imperative to combine the histological and clinical data. Histopathological analysis is not just used to make the diagnostic confirmation, but it is also used to assess the level of the disease and activity in the body. In the context of IBD, the type of mucosal inflammation, destruction, and granulomas or abscesses may contribute to determining the condition of the disease as active or in remission. This difference matters when it comes to customizing the treatment plans, including the application of anti-inflammatory or immunosuppressive drugs during the active phase of the disease, without over-treating in remission.

Conclusion

Histological examination of colonic biopsies plays a pivotal role in the diagnosis, classification, and management of inflammatory bowel disease (IBD) and other related gastrointestinal disorders. The ability to identify characteristic features such as granulomas, cryptitis, crypt abscesses, and mucosal ulceration provides invaluable insight into the underlying pathological mechanisms of disease. These histological markers not only facilitate differentiation between Crohn's disease and ulcerative colitis but also help in assessing disease activity, guiding appropriate therapeutic strategies. Granulomas and transmural inflammation are key indicators of Crohn's disease, while cryptitis, mucosal ulceration, and crypt abscesses are more commonly associated with ulcerative colitis.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-24)
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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

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FJ (Consultant)
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ASC (Professor)
Study Design, manuscript review, and critical input.
SZ (Head of Histopathology Department),
Manuscript drafting, Study Design,

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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