HISTOPATHOLOGICAL INDICATORS OF RELAPSE IN ULCERATIVE COLITIS

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Abstract

Background and Objective: The incidence of inflammatory bowel disease (IBD) which immune-mediated disease is persistently increasing worldwide. It is also associated with an increased incidence of various gastrointestinal carcinomas. The histopathological diagnosis aids in determining the options for treatment, the prognosis of the disease, and the follow-up. The objective of study is to find the frequencies of various histopathological parameters in relapsed ulcerative colitis follow-up patients.

Methods: It was a cross-sectional study conducted Histopathology Department at Sheikh Zayed hospital Lahore from 1/6/2014 to 1/12/2014. Two hundred and seventy patients' colonic biopsies were collected. Patients previously diagnosed with ulcerative colitis of both gender 11 to 80 years old were included. Biopsy specimens in 10% formalin were received. Processing was done and sections were stained with hematoxylin and examined by the pathologist. Data were analyzed by the SPSS version 15.

Results: All 270 patients had chronic inflammation and an increased number of neutrophils in lamina propria. Focal lymphoid aggregate in 162/270(60%), increased number of eosinophils in lamina propria in 108/270(40%), Cryptitis in 216/270(80%), crypt distortion in 202/270(75%), mucin depletion in151/270 (56%) and crypt abscess formation in 148/270(55%) were seen.

Conclusion: Cryptitis and crypt abscess were seen to be the most commonly occurring indicators of relapse in ulcerative colitis.

Keywords: Ulcerative colitis, Relapsed, Histopathology

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The incidence of inflammatory bowel disease (IBD) which immune-mediated disease is persistently increasing worldwide. It is more common in females and early teens and twenties. There are two major forms of it i.e. Crohn's disease and ulcerative colitis[1]. Crohn's disease can cause transmural inflammation and affect any part of the gastrointestinal tract most commonly, the terminal ileum or the perianal region in a non-continuous manner. Whereas, Ulcerative colitis is a chronic disease characterized by remitting recurring inflammation which primarily involves the rectum and spreads from the distal to the proximal colon. This is a worldwide disease and its course varies geographically. Individualized diagnostic and therapeutic management is required because of the variable course of the disease.[2] The risk of developing dysplasia and then cancer increases with the increasing duration of the disease. The histopathological diagnosis also aids in determining the options for treatment, the prognosis of the disease, and the follow-up. The aim of diagnosis is to differentiate inflammatory bowel diseases from the other types of colitis, differentiate between ulcerative colitis and Crohn's disease, and also to identify dysplastic lesions.

There are multiple risk factors involved in pathogenesis like HLA association the ADCY7 gene has

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the strongest association with UC. Other factors include immunological factors, depletion of protective microbiota, impaired epithelial barrier, and environment westernization. Appendicitis and smoking are protective against ulcerative colitis[3]. Morphologically disease can be categorized into acute and quiescent phases with a resolving phase in between. The microscopically active phase of ulcerative colitis shows depleted mucin in the colonic epithelium, cryptic hyperplasia, elongation, branching, and distortion. In the lamina propria mixed acute and chronic inflammatory cell infiltrate with an increased number of eosinophils and mast cells, lymphoid follicles, and edema with congestion are seen. Most diagnostic features like cryptitis and crypt abscess formation are observed in active disease. The inactive or the quiescent phase shows mucosal atrophy, crypt shortening, and a reduced number of crypts per unit length of the mucosa. The lamina propria shows chronic inflammatory cell infiltrate comprising of lymphocytes and plasma cells.[4] The resolving phase shows the return of a normal number of goblet cells with normal surface epithelial cell configuration. Crypt distortion and shortening may be seen. The number of acute inflammatory cells especially neutrophils is decreased. Occasional crypt abscess formation can be identified. Chronicity leads to colonic epithelial cell hyperplasia in ulcerative colitis due to which cell turnover increases which leads to dysplasia and malignancy in longstanding cases. Relapsed ulcerative colitis is defined as when cryptitis and the crypt abscess are identified on microscopy within one year or less after the disease remission.

Multiple statistical pieces of evidence indicate that histologic activity assessment can accurately predict clinical relapse, hospitalization, corticosteroid use, and the development of dysplasia[5]. The histopathological parameters can aid in differentiating neoplastic and non-neoplastic lesions and also can facilitate in early detection of colorectal cancer.[6] The therapy is based upon induction and maintenance of remission. The pathologist can play a significant role by providing proper knowledge about the disease pattern which helps in making further decisions about the therapeutic management and follow-up of patients. The current goal of treatment of ulcerative colitis is endoscopic and ultimately histological healing of mucosa.[7]

METHODS

This cross-sectional study was conducted for six months duration from 1/6/2014 to 1/12/2014 in the Histopathology department of Sheikh Zayed hospital Lahore. It included 270 patients undergoing endoscopic evaluation. These patients were 11 years or above, both genders, and already diagnosed cases of ulcerative colitis presenting with relapse. Patients having a complete set of colonic and rectal biopsies were included. The patient who refused to give informed consent were excluded from the study. Colonic biopsy specimens were taken from these three sites i.e. proximal colon, distal colon, and rectum during colonoscopy follow-up evaluation.

Specimens were collected in three separate containers and fixed in 10% buffered formalin. The tissues were passed totally in three blocks. Then they were processed all overnight in an automated tissue processor (Shandon) and the paraffin-embedded blocks were formed. Two sections were cut at a 3-5 micrometer using a microtome. They were stained with routine Hematoxylin and Eosin stains. Seven histologic parameters were assessed i.e. neutrophils and eosinophils in lamina propria, chronic inflammation, basal lymphoid aggregate, cryptitis, mucin depletion, crypt distortion, and crypt abscess, and recorded in the proforma. The whole study was done by one observer.

All of the data was entered and analyzed by SPSS version 15. Age was described by using mean and standard deviation while gender as frequency and percentages. The histological findings regarding the presence of cryptitis, crypt distortion, crypt destruction, crypt abscess, mucin depletion, chronic inflammation, basal lymphoid aggregate, eosinophils, and neutrophils in lamina propria was also summarized as frequency and percentages.

RESULTS

The present study included 270 patients with

ulcerative colitis in Sheikh Zayed Hospital, Lahore, and subsequently had their endoscopic biopsies submitted for histopathological evaluation in the Department of Histopathology. Two hundred and seventy patients were recruited in this study, the age range was between 11 to 80 years. Out of this, 120 were males and the mean age was 39.24± 15.64 years (Figure-1). The male-to-female ratio was 1:1.25. Figure-2 shows microscopic abnormalities that were common in the biopsy specimens which were taken into this study. All the specimens have shown the presence of chronic inflammation and an increased number of neutrophils in lamina propria (100%), 162 had focal lymphoid aggregate (60%), 108 showed an increased number of eosinophils in lamina propria (40%), 216 had cryptitis (80%),202 have shown crypt distortion (75%), crypt abscess formation in 148(55%) and mucin depletion in 151 (56%) of the cases.

Table 1: *Showing frequencies of various histopathological indicators of relapsed ulcerative colitis (n= 270).*

Histopathological Indicators	No. Of Cases	Percentage (%)
Chronic Inflammation and Increased Number of Neutrophils in Lamina Propria	270	100%
Lymphoid Aggregate	162	60%
Increased Number of Eosinophils	108	40%
Cryptitis	216	80%
Crypt Distortion	202	75%
Crypt Abscess	148	55%
Mucin Depletion	151	56%

Table 2: *Age distribution of the patients presenting with relapse of ulcerative Colitis (n=270)*

Age of patients (years)	Frequency (*f*)	Percentage (%)
11-20	26	10%
21-30	74	27%
31-40	63	23%
41-50	49	18%
51-60	32	13%
61-70	16	2%
71-80	10	4%

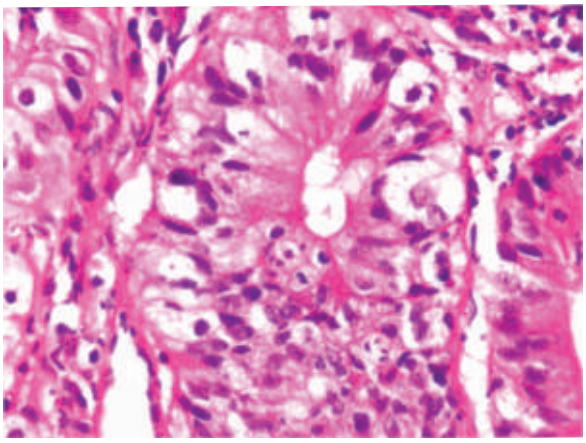

Figure # 1: *Photomicrograph shows active inflammation in colonic mucosa with neutrophilic infiltration in crypts (cryptitis). (H&E stainx115).*

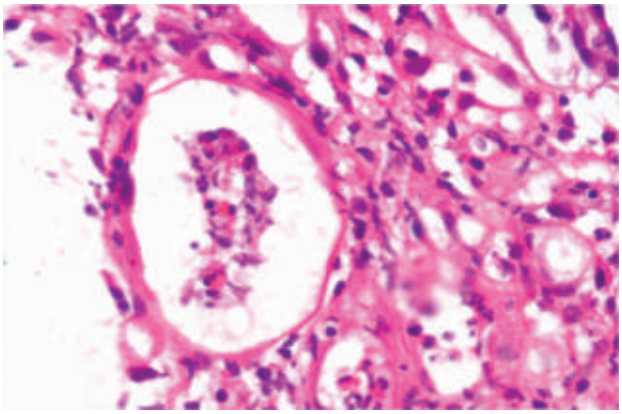

Figure # 13: *Photomicrograph shows crypt abscess formation. (H&E stainx115).*

DISCUSSION

Ulcerative colitis is a disease characterized by mucosal involvement beginning in the rectum and extending proximal to involve all or part of the remaining colon. Biopsies are helpful in diagnosing the cases of known cases of ulcerative colitis with normal-looking mucosa because sometimes normal-looking mucosa may show obvious signs of disease activity. In the active phase of ulcerative colitis reported in studies done in different regions of the world have shown cryptitis. Other superimposed features of activity include intense mucosal inflammation with crypt abscess formation and mucin depletion in goblet cells. In this study, out of 270 majorities of patients were seen in the age group 21-40, and the mean calculated age was 45.5 years.

Similarly, Alain Bitton et al observed 40 years mean age and predominately females in their study[8]. Another study reported median age of 47 years and 53% were men[9]. One of the studies reported a mean age of 48.8 ±14.3[10]. Hence these findings are quite similar to our study. A study showed infiltration of the lamina propria by eosinophils and neutrophils (13/15, 86.6%), cryptitis (14/15, 93.3%), and crypt abscesses (8/15, 53.3%).[11] In Dayanand Medical College and hospital India, a study carried out in which cryptitis was found to be noted in 53.33%, crypt abscess in 6.67%, basal lymphoid aggregate in 60%, crypt distortion, and chronic inflammation in 100%, neutrophils in lamina propria 66% and eosinophil in lamina in 73% of relapsed cases.[12] Another study done in TN Medical college Mumbai showed neutrophils in lamina propria in 38%, cryptitis in 97.2%, lymphoid aggregate in 50.9%, eosinophils I lamina propria in 6.36%, crypt distortion in 69.7% crypt abscess in 69.7%.[13] Another study observed that 64.4% of the cases showed infiltration of the lamina propria by eosinophils and neutrophils cryptitis in 32.2%, mucin depletion in 41.1%, and crypt abscesses in 31.3% of biopsies.[14] Different international studies have reported variations in their frequencies due to variable courses of disease in different parts of the world. The presence of crypt abscess formation is reliable for the evidence of disease activity. The infiltrations of polymorphonuclear neutrophils in crypts forming the crypt abscess are also a feature of the active phase or the relapse of ulcerative colitis. It is important to realize that cryptitis and crypt abscesses can also occur due to numerous other causes like infections or other forms of colitis. Thus, they indicate the disease activity rather than the underlying etiology. The presence of other indicators also helps in confirming the diagnosis of ulcerative colitis. In my experience crypt abscess is an important indicator of acute phase ulcerative colitis and was seen in 55% of cases of the active phase of the disease. Mucin depletion is also a characteristic and fairly consistent finding in active ulcerative colitis.

CONCLUSION

Among all the histopathological indicators, cryptitis and crypt abscess formation were found to be the most commonly found indicators for diagnosing relapse in ulcerative colitis.

Conflict of Interest *None*

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REFERENCES

1. Zhang YZ, Li YY. Inflammatory bowel disease: Pathogenesis. World J Gastroenterol. 2014 January 7; 20 (1): 91-9.
2. Cornaggia M, Leutner M, Mescoli C, Sturniolo GC, Gullotta R. Chronic idiopathic inflammatory bowel disease: The histological report. Digestive and Liver disease 2011; 293-303.
3. Porter RJ, Kalla R, Ho GT. Ulcerative colitis: Recent advances in the understanding of disease pathogenesis. 2020 Apr 24; 9
4. Yamamoto-FurushoJK, Martínez-Benítez B, Sánchez-Morales G . Histological parameters at diagnosis as early predictors of histologic remission along the course of ulcerative colitis. Gastroenterology Research and Practice Volume 2020, Article ID 8891937, 5 pages
5. Pai RK, Jairath V, Vande Casteele N, Rieder F, Parker CE, Lauwers GY. The emerging role of histologic disease activity assessment in ulcerative colitis. Gastrointes Endosc . 2018 Dec;88(6):887-898
6. Ullman T, Odza R, Francis A Farraye. Diagnosis and management of dysplasia in patients with ulcerative colitis and Crohn's disease of colon. Inflamm bowel disease 2009; 15:63
7. S A Riley, V Mani, M J Goodman, S Dutt, M E Herd. Microscopic activity in ulcerative colitis: what does it mean? Gut, 1991, 32,174-178
8. Bitton A, Peppercorn MA, Antonioli DA, Niles JL, Shah S, Bousvaros A, Ransil B, Wild G, Cohen A, Edwardes MD, Stevens AC. Clinical, biological, and histologic parameters as predictors of relapse in ulcerative colitis. Gastroenterology. 2001 Jan; 120(1):13-20.
9. Bessissow T, Lemmens B, Ferrante M, Bisschops R, Van Steen K, Geboes K, Van Assche G, Vermeire S, Rutgeerts P, De Hertogh G. Prognostic value of serologic and histologic markers on clinical relapse in ulcerative colitis patients with mucosal healing. Am J Gastroenterol. 2012 Nov; 107(11):1684-92.
10. Toyonaga T, Saito E, Hisamatsu T, Hibia. Histological Risk Factors to Predict Clinical Relapse in Ulcerative.

Journal of Crohn's and Colitis, 2018, 1288–1294

11. Narang V, kaur R, Garg B, Mahajan R, Midha R, Sood N. Association of endocopic and histological remission with clinical course in patients of ulcerative colitis. Intest Res.2018 Jan 16(1)55.61
12. Hussainy AS, Jafri W, Sheikh H .A Histopathological study comparing western and Pakistani Idiopathic Ulcerative Colitis. Pak J Pathol 1991; 2(1):23-7.
13. Azad S, Sood N and Sood A. Biological and histological parameters as predictors of relapse in ulcerative colitis. Saudi J Gastroenterol 2011; 17:194-8.
14. Ozaki R, Kobayashi T, Okabayashi S, Nakano M, Morinaga S, Hara A, Ohbu M, Matsuoka K, Toyonaga T, Saito E, Hisamatsu T, Hibi T. Histological Risk Factors to Predict Clinical Relapse in Ulcerative Colitis With Endoscopically Normal Mucosa. J Crohns Colitis. 2018 Nov 15; 12