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Original Article

Histopathological evaluation of ulcerative colitis in colonoscopic biopsies

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ABSTRACT

Background: Histopathologic evaluation of colonoscopic mucosal biopsy remains one of the earliest modalities of investigation in patients clinically suspected of ulcerative colitis. Pathologists should be aware of classical histomorphological features to avoid misdiagnosis. The aim of the present study was to evaluate histopathologic features as well as to determine possible atypical presentation.

Materials and Methods: Forty newly diagnosed cases of ulcerative colitis were included in the study. Colonoscopic biopsies taken from rectum as well as various areas of colon and ileum depending upon clinical extent of involvement were submitted for histopathological evaluation. Diagnosis of ulcerative colitis was made by correlating clinical, endoscopic and histopathologic findings.

Results: Out of 47 cases suspected of ulcerative colitis, histopathologic features were consistent with Ulcerative colitis in 40 cases. Almost all cases (97.5%) showed diffuse active colitis. Cryptitis (100%), crypt abscesses (75%) and basal plasmacytosis (85%) along with crypt architectural abnormalities (75%) and goblet cell depletion (70%) were classical histological changes associated with ulcerative colitis in active phase. Atypical presentations noticed were focal active colitis (2.5%), backwash ileitis (2.5%), rectal sparing (2.5%) and skip areas (5%).

Conclusion: Accurate diagnosis of ulcerative colitis requires elaborate knowledge of histopathologic features along with awareness of possible atypical presentation.

INTRODUCTION

Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) of unknown cause.[1] A precise diagnosis of UC is of paramount importance for appropriate treatment. The diagnosis of IBD requires a multidisciplinary approach involving a team of specialists (eg, gastroenterologists, pathologists and radiologists). The diagnosis should be established by a combination of medical history, clinical evaluation, laboratory data (including negative stool examinations for infectious agents) and typical endoscopic, histologic and radiologic findings. Histologic examination of endoscopic biopsies remains a key step in the work-up of affected patients and can be used for diagnosis and differential diagnosis, particularly in the differentiation of UC from Crohn's disease (CD) and other non-IBD related colitides.[2] One of the earliest mode of histological

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Table 1: Extent of bowel involvement by ulcerative colitis on colonoscopy:

Extent of bowel involvement	Number of cases	% of cases
Left sided disease with rectal involvement	22	55
Left sided disease with rectal sparing	1	2.5
Rectal involvement only	11	27.5
Continuous left sided disease with right side involvement	3	7.5
Continuous left sided disease with skip areas on right side	2	5
Pan colitis with backwash ileitis	1	2.5

evaluation is colonoscopic mucosal biopsy. Biopsies also allow assessment of disease activity and identification of pre-cancerous lesions and cancer.[1] Accurate diagnosis requires knowledge of classic morphological features; pathologists should however be aware of the atypical pathologic presentation as well to prevent misdiagnosis.[3] Hence the purpose of our study was to evaluate classic histopathologic features as well as to determine atypical presentations of Ulcerative colitis.

MATERIALS AND METHODS

Forty seven new cases suspected of ulcerative colitis clinically and/ or endoscopically undergoing colonoscopic biopsies at Pathology departments of Kathmandu Hospital Private limited and Kathmandu Medical College- Teaching Hospital from June 2013 to May 2015 were included in the study. Already diagnosed cases and patients who had taken specific medications for colitis or coexisting disease were excluded from the study. Detailed endoscopic findings, extent of disease, clinical disease severity were recorded. Colonoscopic biopsies were taken from rectum as well as various areas of colon depending upon the clinical extent of involvement. Biopsy from terminal ileum was also taken where applicable. Biopsy tissue was immediately fixed in 10% Formalin, processed routinely and stained with Hematoxylin and Eosin stain. Histopathologic parameters assessed were pattern of inflammation, crypt architectural abnormalities, goblet cell depletion, types of inflammatory cells in the lamina propria, basal plasmacytosis and activity (cryptitis and crypt abscesses). The slides were also analysed for presence of dysplasia or any unusual histopathologic features. Statistical analysis was performed using Epi-info wherever necessary.

RESULTS

Out of 47 cases suspected of ulcerative colitis, histopathologic features were consistent with Ulcerative colitis in active phase in 40 cases. Seven cases which showed non-specific inflammatory changes were excluded from the study. Diffuse active colitis, crypt architectural abnormalities with loss of goblet cells and basal plasmacytosis were considered to be the typical histologic features associated with ulcerative colitis.

Most of the patients were between 21 – 40 years of age, the youngest being 21 years and the eldest was 71 years of age. All patients presented with a history of bleeding PR. Most of them also had complains of diarrhoea with passage of stool mixed with mucus (25 cases, 62.5%). Some patients had constipation (7 cases, 17.5%) and abdominal pain (5 cases, 12.5%) while others had non-specific symptoms (3 cases, 7.5%). These symptoms were present for few days to few years. All patients underwent colonoscopy with biopsy. Colonoscopy revealed left sided colitis with rectal involvement in 22 cases (55%). Eleven cases (27.5%) showed rectal involvement only. Rectal sparing was observed in 1 case (2.5%). Continuous left sided disease with right side involvement was noted in three cases (7.5%) while skip areas were observed on right side in two cases (5%). One case presented with pancolitis with backwash ileitis (2.5%). (Table 1; fig. 1)

Among the forty cases, 26 (65%) had mild colitis, eight (20%) had moderate colitis and six (15%) had colitis of severe degree endoscopically. Pseudopolyps were noted in four (10%) of these cases.

Histologic evaluation revealed diffuse active colitis in almost all cases (39 cases, 97.5%) except one (2.5%) which showed focal active colitis. 15 cases (37.5%) showed mild distortion of crypt architecture while 13 (32.5%) showed moderate distortion and two cases (5%) showed marked distortion with crypt atrophy. In 10 cases (25%) crypt architecture appeared normal. Goblet cell depletion was noted in 28 cases (70%). The predominant cells in the lamina propria were lymphocytes and plasma cells. Basal plasmacytosis (fig. 2) was present in 34 cases (85%). Lymphoid follicles were observed in 10 cases (25%). Eosinophils were prominent in 27 cases (67.5%). Cryptitis was present in all cases (100%) whereas crypt abscesses (fig. 3) were detected in only 30 cases (75%). Muscularis mucosal hypertrophy was appreciated in 8 cases (20%). Low grade dysplasia was present in one case (2.5%). None of the cases had invasive carcinoma. (Table. 2)

DISCUSSION

The histologic diagnosis of IBD is based on analysis of a full series of colonoscopic biopsies. A study by Dejaco et al. showed that the accuracy of diagnosing colitis increases from 66% to 92% when segmental biopsies are taken rather than two biopsies throughout the colon.[4] Rectal biopsies are necessary to either confirm or reject rectal involvement and may be additionally helpful in differentiating IBD from other inflammatory lesions.[2]

All tissue samples should be fixed immediately by immersion

Table 2: Histopathologic features of Ulcerative colitis

Histopathologic features	Number of cases	% of cases
Crypt architecture		
Normal	10	25
Mild distortion	15	37.5
Moderate distortion	13	32.5
Marked distortion	2	5
Goblet cells		
Depleted	28	70
Preserved	12	30
Basal plasmacytosis		
Present	34	85
Absent	6	15
Cryptitis		
Present	40	100
Absent	0	0
Crypt abscesses		
Present	30	75
Absent	10	25
Eosinophilic infiltrate		
Prominent	27	67.5
Not prominent	13	32.5
Lymphoid follicles		
Present	10	25
Absent	30	75
Muscularis mucosal hypertrophy		
Present	8	20
Absent	32	80
Pseudopolyps		
Present	4	10
Absent	36	90
Dysplasia		
Low grade	1	2.5
High grade	0	0
Absent	39	97.5

in buffered formalin or an equivalent solution prior to transport. Serial sectioning of biopsy specimens is superior to step sectioning in order to detect mild or focal lesion and to increase the diagnostic accuracy.[5-7] The diagnostic yield increases with the number of sections examined. However the ideal number of sections to be examined in routine practice has not been established with numbers varying between 2 and 6 in different studies.[6,8]

Ulcerative colitis classically shows a diffuse and continuous chronic inflammation without skip areas which involves the rectum and spreads proximally with gradually decreasing severity of inflammation. Unusual inflammation patterns are rectal sparing, caecal patch and backwash ileitis.[2] Our study also demonstrated one case (2.5%) of rectal sparing, one (2.5%) with backwash ileitis and two (5%) with skip lesions. Although rectal sparing and patchy disease suggest diagnosis of Crohn's disease, the cases included in our study showed diffuse active colitis on histology favoring ulcerative colitis. Many studies have attributed rectal sparing and skip lesions to either local use of steroids or oral medications.[9-13] We however included only those patients who did not receive any form of medical therapy prior to initial endoscopic procedure. Hence, it should be emphasized that awareness of unusual macroscopic distribution patterns, such as skip lesions, rectal sparing and backwash ileitis is important to avoid wrong subtyping of the inflammatory bowel disease.

Untreated UC in an active phase represents the prototypic diffuse active colitis. Biopsy specimens usually demonstrate a diffuse abnormality, meaning that the changes are of approximately the same intensity in all areas of the tissue.[14] We observed diffuse active colitis in almost all cases (39, 97.5%) although the degree of architectural distortion and degree of inflammation varied in different cases. One of the cases however showed focal active colitis. Clinical presentation, endoscopic findings and other histopathologic features favored ulcerative colitis over Crohn's Disease in this case. Diffuse active colitis though diagnostic of UC can also be seen in some examples of Crohn's colitis and in some cases of documented infectious colitis, although the latter could represent an infectious exacerbation of underlying latent primary inflammatory bowel disease. The diffuse active colitis pattern can also be seen in a form of colitis associated with diverticular disease; this entity is distinguished from classic UC by its rectal sparing and its presence exclusively in areas of diverticula.[14]

Focal active colitis refers to the patchy distribution of combined architectural change and inflammation in a mucosal biopsy specimen. The focal active colitis pattern consists of limited areas of increased inflammatory cells associated with focal architectural distortion; characteristically, some areas of the biopsy specimen maintain an essentially normal appearance. The focal active colitis pattern is usually not seen with UC, and, when it is present, suggests Crohn's colitis or infectious colitis and/or acute self-limited colitis. However, the focal active colitis pattern can be seen in resolving UC under medical treatment, and areas of previously inflamed colon and rectum in UC can return to an almost normal histologic appearance.[14-16]

Microscopic diagnosis of UC is based on widespread crypt architectural distortion, a diffuse transmucosal inflammatory infiltrate with basal plasmacytosis, eventually associated with an active component, causing cryptitis and crypt abscesses. Goblet cell depletion is less specific, but a helpful diagnostic feature.[2] We observed variable degree of crypt architectural distortion in the form of crypt branching and budding and crypt atrophy. Various studies have shown distorted crypt architecture ranging from

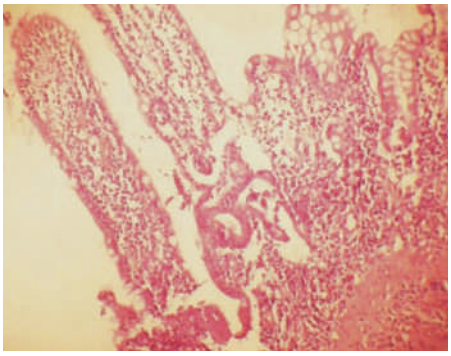

Figure 1: *lleal biopsy showing backwash ileitis (HE stain, X100).*

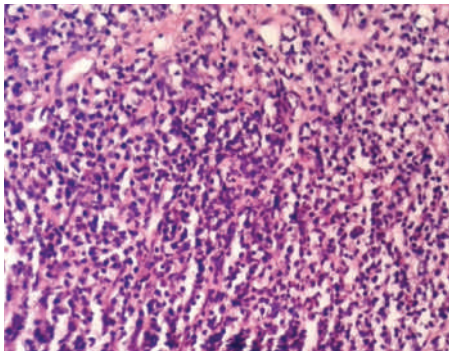

Figure 2. *Colonic biopsy showing Basal plasmacytosis (HE stain, X400).*

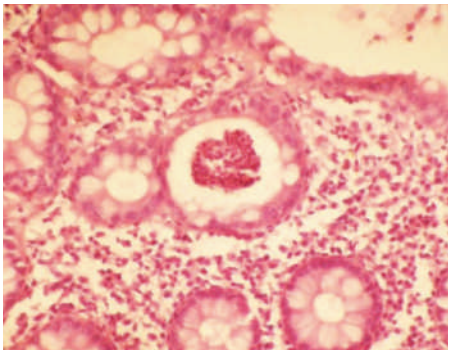

Figure 3: *Rectal biopsy showing crypt abscess and diffuse lymphoplasmacytic infiltrate in the lamina propria (HE stain X400).*

57 to 100% of cases.[17-20] However in long standing cases restoration of architecture may result in a normal mucosa.[14] We noticed normal crypt architecture in ten cases (25%). The inflammatory infiltrate was composed of lymphocytes, plasma cells, neutrophils and eosinophils. Plasma cells are predominantly observed in between the crypts and the muscularis mucosae (basal plasmacytosis) which is the earliest diagnostic feature with the highest predictive value for the diagnosis of UC.[14] In our study also, basal plasmacytosis was a constant feature (present in 34 cases). Basal plasmacytosis is helpful in the differentiation between a first attack of UC and infectious colitis, but not CD. Cryptitis as defined by presence of neutrophils within crypt epithelium and crypt abscesses defined by the presence of neutrophils within crypt lumina are features suggestive of active inflammation.[14,17,19]

Eosinophil infiltrate was prominent in 27 cases. There has been increasing evidence about the involvement of eosinophils in the pathogenesis of inflammatory bowel disease. Eosinophils play an important role as pro-inflammatory and pro-motility agents thus producing diarrhoea, tissue destruction and fibrosis.[21]

Inflammation may cause mucin depletion of the epithelium, a less diagnostic feature as it can also be found in infectious colitis and CD. We observed goblet cell depletion in 20 cases. Ajioka et al have reported that in the remission phase of ulcerative colitis inflammation is reduced and goblet cell mucus is reduced however evidence of past inflammation such as irregular crypts, paneth cell metaplasia and muscularis mucosa hypertrophy can still be appreciated.[14,22]

Preserved crypt architecture and the absence of a transmucosal inflammatory cell infiltrate do not rule out ulcerative colitis at an early stage. Le Berre et al. have shown that distorted crypt architecture with crypt atrophy, mucin depletion and cryptitis are features highly predictive of UC. Nevertheless features may change depending upon disease duration, patient's age and treatment. Hence it is recommended that rather than individual histomorphological features, combination of these changes need to be considered before giving the diagnosis of UC.[2,23]

Atypical presentation in UC is not uncommon. We noted one case with rectal sparing. Review of current literature reveals that in long standing disease the extent of gut involvement decreases with time ultimately leading to complete restoration of the rectal mucosa (rectal sparing) in 34 to 44% of patients.[13,24] Our patient gave history of per rectal bleeding for 2 years before the first colonoscopy attempted, hence rectal sparing can probably be attributed to long history of ulcerative colitis.

One of the cases had pancolitis with involvement of ileum (backwash ileitis). It has been known that ulcerative colitis can spread to other portions of the gastrointestinal tract. Review of literature shows that ileum is involved in approximately one third of cases. This involvement is always in continuity with the colonic disease; it rarely spreads more than 10 cm away from Ileocaecal valve.[25]

In our study we observed only one case (2.5%) showing low grade dysplasia. No invasive carcinoma was detected. Studies have shown colorectal cancer risk is associated with disease duration and disease extent and raises at the rate of approx. 0.5 to 1% per year after a total duration of colitis of 8 to 10 years.[26-28] The incidence of dysplasia or malignancy

may appear lower in present study as we included only newly diagnosed cases. An elaborative study with regular follow up biopsies is required to understand the true risk for dysplasia or malignancy associated with ulcerative colitis.

CONSLUSION

Accurate diagnosis of UC requires elaborate knowledge of histological features. The histological findings should be correlated with clinical and endoscopic findings. Pathologists should also be aware of possible atypical presentation.

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