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ORIGINAL ARTICLE

Clinical Features and Histological Features of Relapsed Patients of Ulcerative Colitis

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ABSTRACT

Introduction: Ulcerative colitis is a chronic inflammatory disease of indefinite etiology having relapsing and remitting course. Assessing inflammatory activity via different scoring systems along with clinical correlation plays an important role in the diagnosis and surveillance of ulcerative colitis patients. Histopathological findings should be correlated with the clinical, endoscopic and radiological findings to exclude other causes with similar symptomatology, hence improving the management of patients with UC.

Aims and objective: To determine the clinical features and histological features in relapsed patients of ulcerative colitis.

Place and duration of study: Department of Pathology, Histopathology section, Sheikh Zayed hospital Lahore, from 25th February, 2016 to 25th February, 2017.

Materials and methods: One hundred and ninety cases underwent endoscopic colonic biopsies from the three sites proximal colon, distal colon and rectum.

Results: Out of one hundred ninety patients majority patients presented with vague abdominal pain 105(55.3%) followed by bleeding per rectum 74(38.9%). Most commonly seen histological feature is cryptitis 189(99.5%) succeeding chronic inflammation 188 (98.9%).

Conclusion: Relapsed patients predominantly presents with vague abdominal pain. Cryptitis is most commonly seen histological feature in relapsed patients of ulcerative colitis.

Keywords: Inflammatory bowel disease, Ulcerative colitis , Crohn's disease

INTRODUCTION

Inflammatory bowel diseases (IBD) are lifelong disorders of undefined etiologies in developed countries. IBD encompasses two diseases Ulcerative colitis (UC) and Crohn disease (CD) with distinct and overlapping clinicopathological features. The incidence of UC has been increased in western countries after World War II [1]. The reported incidence of UC in Asia is 0.4 to 2.1/100000 and prevalence rate is 6 to 30/100000population with equal gender distribution [2,3]. The reported incidence of UC is 214/100,000 in a population based study in Minnesota Omlsted country [4].

The etiology of UC is unknown and incompletely understood. Multiple factors are responsible for pathogenesis. UC is a polygenetic disease with genetic factors such as single nucleotide polymorphisms, mutations in genes responsible for autophagy such as ATG16L1, IRGM, IL23R and NOD2 receptor are well documented. Multiple environmental risk factors such as smoking, diet, drugs, social and psychological stressors are described to play a part. Apart from these factors aspirin and NSAIDS can trigger onset and relapse of UC [5].

In first two weeks of embryo, gut microflora composed of 1150 bacterial species is formed. It is suggested that the altered luminal bacteria and enhanced intestinal permeability is responsible for dysregulation of intestinal immunity. The immunological factors responsible for UC are aberrant or dysregulated T cells. It is explained by hygiene hypothesis which states that individuals less exposed to infections during childhood or unpolluted conditions loose the ability to regulate T cell development, unable to develop sufficient immune response and aberrant intestinal inflammatory response due to over activation of Th2 response [6].

UC can present with fever, lack of appetite, weight loss and fatigue. Clinically, digestive tract symptoms are diarrhea, constipation, rectal bleeding, altered bowel habits, heavy mucus discharge, tenesmus and bloating abdominal pains. UC can present with other autoimmune diseases like Primary Sclerosing Cholangitis, Multiple Sclerosis and Bullous skin disorders. There is regional variation in symptomatology for example in Pakistan and India extra intestinal manifestations are relatively uncommon in patients of UC [1,2].

Laboratory evaluation of patients include stool examination, CBC, ESR, CRP and p-ANCA. In UC patients ileocolonoscopic examination with two biopsies from five different sites including terminal ileum and rectum is recommended to determine extent and severity of disease rather than rectoscopy alone [7,8]. Histological evaluation before any treatment is very crucial owing to the morphological changes in the colonic mucosa by immunomodulatory agents [9]. Surveillance endoscopies are done in relapsing and remitting patients of UC in which any visible endoscopic lesions are sampled, colorectal neoplasia and efficacies of biological therapies are assessed. Hajime et al showed that use of magnifying endoscopy with vital staining is highly recommended to predict long term outcomes of UC patients and risk of colorectal neoplasia. Fulminant colitis is contraindication of colonoscopy [10,11].

The microscopic diagnostic criteria of untreated UC is segmental distribution of chronic active colitis. Hallmark features of chronicity are widespread crypt architectural distortion and basal plasmacytosis. Histological features of chronicity is crypt distortion which is characterized by shortening, distortion, bifurcation and branching of crypts. Basal plasmacytosis is characterized by separation of base of crypts and muscularis mucosae by lymphoplasmacytic inflammation in oriented sections. Other features of chronicity include grossly visible inflammatory pseudo polyps and microscopically paneth cell metaplasia in sigmoid colon and hypertrophy of muscularis mucosae. Activity is characterized by the presence of crptitis and crypt abscess. Crypt abscesses are characterized by accumulation of neutrophils in the the lumen of crypts and crptitis is characterized by neutrophils invading the wall of crypts .The treated cases of UC shows rectal sparing, uneven healing of mucosa and patchiness of inflammation endoscopically and histologically [8].

Surgical gross colorectal resection specimens show continuous rectal inflammation extending proximally and inflammation decreases gradually with sharp transitions, no skip areas, fissures and ulcers. Mucosa is friable and granular in appearance with majority superficial ulcers and few deep well like ulcers. Inflammatory pseudo polyps are commonly seen in sigmoid and descending colon [9].

It is very important to differentiate UC from CD, infectious colitis (IC), medication induced colitis (MIC), chronic ischemia (CI)

and diverticular associated colitis (DAC) owing to overlapping clinical symptomatology. Clinically patient presents with vague abdominal pain, rectal bleeding, mucus in stool and perianal fistulaes. CD commonly involves ileum. Grossly there is cobble stone appearance of mucosa, wall thickening, deep ulcers, fat wrapping and strictures. Histologically there is crypt architectural irregularity but no crypt distortion is seen. There is patchy chronic inflammation in lamina propria within same site and intervening mucosal sites. In addition lymphoid aggregates, non cryptolytic granulomas, neuronal hyperplasia and muscle hypertrophy are also found. Histologically UC differentiates from IC by the features of chronicity, diffuse uniform chronic active colitis with universal involvement of rectum and absence of granulomas[12].

Histological evaluation of diagnosed patients of UC is very tricky as treatment decreases rectal inflammation, uneven healing of mucosa, patchy inflammation in lamina propria and normalization of rectal mucosa even rectal sparing. Management of UC consists of medical and surgical interventions. Aminosalicylates, anti-inflammatory agents, corticosteroids, immune modifiers, mesalzine, and cyclosporines produces tremendous effect on mucosa causing histological healing . Surgical intervention is done if medical treatment is not successful then temporary ileostomy, total proctocolectomy and ileal-pouch anal anastomosis are done [1].

UC can also present in pediatric age group less than 18 years. The gold standard for diagnosing pediatric UC patients is upper and lower gastrointestinal tract endoscopy with biopsies. Histologically patients can present with normal colonic mucosa and patchiness of inflammation. There is rectal sparing and basal plasmacytosis is relatively less common in children [13].

Aims and objectives: To determine different clinical and histological features in the relapsed patients of ulcerative colitis.

MATERIALS AND METHODS

This study was conducted in the Department of Histopathology, sheikh Zayed hospital Lahore from February 25,2016 to February 25,2017 approved by ethical review board vide its letter number 1406 dated 15/03/2016.

Inclusion criteria: Out door, both genders of known patients of ulcerative colitis of 20 to 70 years age.

Exclusion criteria: Colorectal biopsies showing dysplasia, colorectal neoplasia and patients on endoscopic and clinical remission.

Mucosal tissue biopsies were processed in the automatic tissue processor for 16 hours overnight dehydrated with ethyl alcohol, cleared by xylene, impregnated with paraffin wax and later on tissue blocks were made. Hematoxylin and eosin stains were done.

Statistical analysis: Qualitative data like presenting complains vague abdominal pains, altered bowel habits, passage of mucus stool, per rectal bleed, mucus and anemia in different age groups of patients were presented as frequencies and percentages.Qualitative variables like histopathological features cryptitis, crypt abscess, crypt distortion, basal lymphoid aggregate, neutrophils in lamina propria, eosinophils in lamina propria and diffuse basal plasma cells were presented as frequencies and percentages.

RESULTS

In the present study, out of 190 ulcerative colitis patients there were 117(61.6%) males and 73(38.4%) were females. Predominant patients 64(33.7%) were seen in 31-45 age group and less number of patients 23(12.1%) were seen >60 age group. Mean calculated age was 39.98±16.34 with 15, 82 and 27 as minimum, maximum ages and inter quartile range presented in figure I.

The most common presenting complaint of UC patients is vague abdominal pain 105(55.3%) most commonly seen in 31-45 age group. Per rectal bleeding 74(38.9%) presented more frequently in 15-30 age group. Rest of the presenting complaints are presented in Table 1.

Table 1: Frequency Distribution of Presenting Complaints in different age groups

Age groups					
	15-30	31-45	46-60	>60	Total
Vague Abdominal Pain					
Yes	28	31	29	17	105(55.3%)
No	33	33	13	6	85(44.7%)
Per Rectal Bleed					
Yes	29	27	13	5	74(38.9%)
No	32	37	29	18	116(61.1%)
Diarrhea					
Yes	23	26	10	9	68(35.8%)
No	38	38	32	14	122(64.2.%)
Mucus discharge					
Yes	18	19	12	7	56(29%)
No	43	45	30	16	134(71%)
Altered Bowel Habits					
Yes	12	12	3	5	42(22.1%)
No	49	52	29	18	148(77.9%)
Pale					
Yes	8	11	6	3	28(14.7%)
No	53	53	36	20	162(85.2%)
Anemia					
Yes	1	1	0	0	2(0.1%)
No	61	63	41	23	188(98.9%)
Passage of Mucus Stool					
Yes	1	0	0	0	1(1%)
No	60	64	42	23	189(99%)

Table 2: Frequency Distribution of histological features in different age groups

Age Groups					
	15-30	31-45	46-59	>60	Total
Cryptitis					
Present	61	64	42	22	189(99.5%)
Absent	0	0	0	0	1(0.5%)
Chronic inflammation					
Present	61	64	42	21	188(98.9%)
Absent	0	0	0	2	2(1.1%)
Activity(Neutrophils in lamina propria)					
Present	51	49	33	18	151(79.5%)
Absent	10	15	9	5	39(20.5%)
Crypt distortion					
Present	46	50	22	11	129(67.9%)
Absent	15	14	20	12	61(32.1%)
Crypt Abscess					
Present	45	46	18	12	121(63.7%)
Absent	16	18	24	11	69(36.3%)
Basal lymphocytosis					
Present	31	35	16	8	90(47.4%)
Absent	30	29	28	15	100(52.6%)
Basal lymphoid aggregates					
Present	19	24	12	9	64(33.7%)
Absent	42	40	30	14	166(66.3%)
Eosinophils in lamina propria					
Present	8	8	3	5	24(12.6%)
Absent	53	56	39	18	166(87.4%)

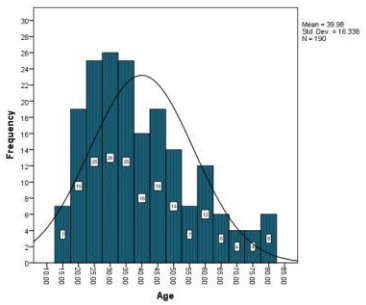

Figure 1: Graphical Presentation of mean, minimum, maximum and IQR of age.

In 31-45 age group, two most common histological features are cryptitis 189(99.5%) followed by chronic inflammation 188(98.9%) shown in figure II,III. Our study showed 151(79.5%) neutrophils in lamina propria and 90(47.4%) basal plasma cells. Rest of the histological features are presented in Table 2.

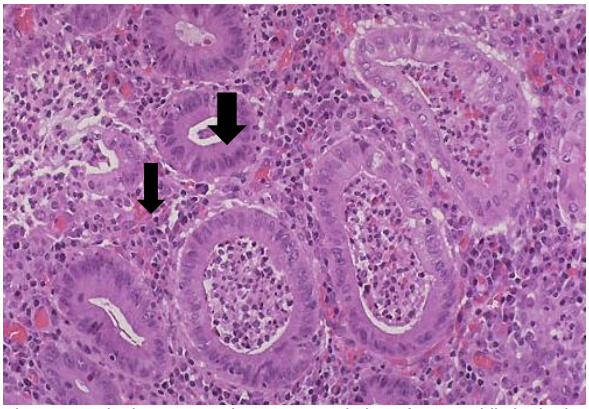

Figure 2: Colonic mucosa shows accumulation of neutrophils in the lumen of crypts highlighted by arrows, Crypt Abscess (400x; H/E)

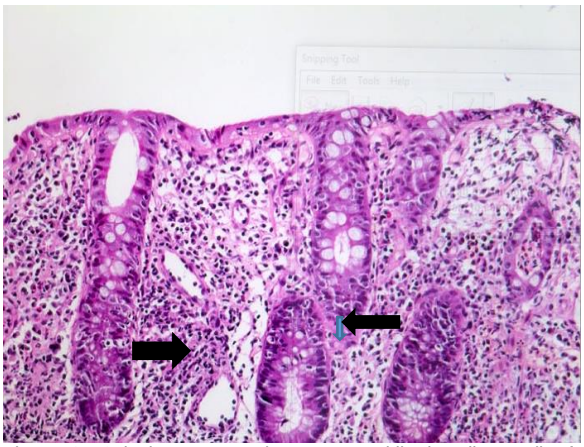

Figure 3: Colonic mucosa shows neutrophils invading wall of crypts highlighted by right arrows ,Cryptitis (400x; H/E)

DISCUSSION

UC is a lifelong chronic debilitating disease consisting of remissions and relapses. Identification of histological features of UC is not only important, however should be interpreted with clinical, endoscopic and radiological findings. The biological treatment of UC has tremendously changed outcome of patients hence improving quality of life[9].

In our study, majority patients 64(33.7%) were seen in 31-45 age group (Figure I) and mean calculated age of all patients was 39.98 years. Similarly Alain Bitton et al noticed 40 years in one year duration [14]. Robert V Bryant et al reported a higher mean age 50 years as compared to our study at six years follow up [15]. Other authors Aranzazu Jauregi Amezagae et al noticed 38years [16]and Petrille Andre Cavalcante De Barros et al reported 37.8 years in a Brazilian population[17].

Regarding sex in our study there were more male patients 117(61.6%).This observation was similar to two studies done by S.A Riley et al 51(54%) [18] and 44 (53%) males [19]. In contrast to our study more females reported by Petrille Andre Cavalcante de Barros et al 28 (70%) [17], Alain Bitton et al 42 (56%) [14] and Aranzazu Jauregi Amezaga 52(50%)[16]. Angela Rochi et al reported slightly higher female incidence by 1.3 [20]. Although studies has proven no gender association in patients of UC.

In our study clinically relapsed patients of UC presented with the most common complain of vague abdominal pain 105.3 (55.3%) similar to Sang Hyoung Park et al164 (53.9%) [21] in contrast Yasmin ozmin et al reported few patients with abdominal pains 70(14.0%) [22]. The second most common presenting complain was rectal bleeding 38.9(70.53%) in contrast Sang Hyoung Park et al 276 (90.8%) and Yasmin ozmin et al 456 (91.2%). Third most common presenting complain in our study was diarrhea 35.8(64.2%) similar to Sang Hyoung Park et al 195 (64.1%). Fourth most common presenting complain is passage of mucoid stool 29.47(70.53%) in contrast to Sang Hyoung Park et al 168 (55.3%)[21,22].

The most common histological feature in our study was cryptitis 189(99.5%) in contrast to other studies by Joshua E. Melson et al 22 (46%) [23], Sheenam Azad et al 8 (53.33%) [24] and Alain Bitton et al 24 % [14]. In our study crypt distortion was 129(67.9%) similar to Aman et al [25] and Alain Bitton et al [14]. In contrast to our study crypt distortion was seen in majority of cases 15(100%) by Sheenam Azad et al [24], 44 (92%) by Joshua E. Melson et al [23] and SA Riley et al [19].

Regarding other microscopic indices crypt abscess was seen in 121(63.7%). In contrast Aman et al 100% [25] and Joshua et al 37 (79%)[23]. Sheenam Azad et al noticed slightly lower frequency of crypt abscess than our study 8(53.3%)[24], SA Riley 9(11%) [19] and Alain Bitton et al [14]. Our study showed 90(47.4%) basal plasma cells in contrast to SA Riley 82(100%) [19]andAranzazu et al 222(65%)[16].

In our study neutrophils in lamina propria was recorded in 151(79.5%) biopsies in contrast to Sheenam Azad et al 10(66.7%) [24] and SA Riley Activity 23(28%) [19]. In our study basal lymphoid aggregates were seen 64(33.7%) of colorectal biopsies. In contrast to other authors Joshua et al 23 (49%) [23]and Sheenam Azad et al 9 (60%), Aman et al [25] and Alain Bitton [14]. In our index study the least seen microscopic feature was eosinophils 24(12.6%) in contrast to Sheenam Azad et al 11(73.3%) [24] and Aman et al 92 % [25].

CONCLUSION

Relapsed UC patients predominantly presented with vague abdominal pains. Cryptitis is most commonly seen histological feature in relapsed patients of ulcerative colitis. There should be a multimodality approach in the surveillance of UC patients.

Conflicts of Interest: There were no conflicts of interest.

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