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Prevalence, Clinical and Histopathological features of Microscopic Colitis in Some Egyptian Patients with Diarrhea-Predominant Irritable Bowel Syndrome

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Abstract: ***Background: Irritable bowel syndrome (IBS) is a common functional gut disorder where its diagnosis can be challenging and uncertain due to presence of many organic diseases that can mimic IBS and one of the commnest these disorders is MC. Patients and methods: 120 patient with diarrhea predominant irritable bowel syndrome (IBS-D) were subjected to full history and physical examination. Colonscopy with multiple biopsies were done for all patients and refered for histopathological examination. Results: Distinct colonscopic findings were found in 19 patient were excluded. 8.9% of patients were diagnosed with lymphocytic colitis (LC) and 1.9% of cases with collagenous colitis (CC) with a mean age of 49 years and women are affected with microscopic colitis (MC) more than men. Nocturnal diarrhea ocurrs in 72.7% of cases with a mean frequency 4 times per day. Conclusions: Clinical presentation alone is not sufficient in differentaition between MC from IBS-D. The hallmark of diagnosis is histopathological diagnosis. Colonscope with multiple biopsies is recommended for all patients with IBS-D.***

Keywords: diarrhea predominant irritable bowel syndrome -microscopic colitis

1. Introduction

Inflammatory and non inflammatory colitides represent a heterogeneous group difficult to diagnose and classify, where their diagnostic criteria are not the same. Moreover, epidemiological data are still relatively scarce, even for the most common entities (1).

Microscopic colitis present clinically by chronic watery diarrhea, with normal colonic mucosa on colonscopy(2) where diagnostic histopathological features are seen on microscopic examination. However, some authors believe that the term MC should not be used by the pathologist (and also by the clinician), because it is a misleading and inconclusive definition for both professional figures, in that it represents a sort of semantic umbrella for two actual entities, namely CC and LC (3).

It is of great importance that the clinician and the pathologist work as a well-integrated team; where the pathologist should receive accurate and detailed clinical information about the clinical problem, in addition to an adequate (at least three samples for each colonic segment, possibly including the terminal ileum, samples taken on both visible lesions and in the near, apparently normal mucosa) (4).

These conditions should be correctly diagnosed to provide a clear direction to help clinicians to better target the treatment, even though these entities may often share important similarities, and probably represent morphologic different phases of one disease process (5).

Irritable bowel syndrome is the commonnest functional gut disorder(6). Since the etiology of IBS is unknown and possibly multifactorial, some overlap in symptoms between IBS and various forms of colitis may exist. Proper diagnosis of IBS may be challenging and uncertain due to absence of specific clinical, laboratory or endoscopic features and the discrepancy in symptoms between different patients and even in the same subject. Many organic diseases can simulate IBS and one of the commnest these disorders is MC (7).

This study was designed to clarify the prevalence, clinical and histopathological features of MC in Egyptian patients with IBS-D.

2. Patients and methods

2.1. Patients

This is a prospective study conducted on 120 patients attending to Gastroentrology clinic, Specialized Medical Hospital, Mansoura University, from January 2016 to July 2017 complaining from IBS-D (according to Rome III criteria) where all patients are subjected to physical examination. In history taking, age, gender, smoking or exsmoker, prescence of diarrhea as regard frequency and characters, abdominal pain, flatulence, weight loss, history of previous recurrent gastroentritis, drug intake specially non steroidal antiinflammatory drugs (NSAIDs) and prescence of comorbidities as type 1 Diabetes mellitus (DM), Rheumaoid arthritis (RA), thyroid diorders, pernicious anemia or scleroderma were recorded. All patients will undergo complete stool examination, liver function tests, serum creatinine and abdominal ultrasound.

Patients with diagnosed organic colonic diseases, hepatic failure, renal disease (creatinine ≥ 2 mg/dL), malignancies or food allergy were excluded.

2.2 Colonscopy

Total Colonscopy by expert gastroentrologist will be for all patients for exclusion of organic diseases and taking colonic biopsy (three samples from each colonic segment) for histopathological examination.

2.3. Biopsy Processing

120 cases of endoscopic colonic biopsy were received, fixed in 10% neutral buffered formalin. After counting the number of fragments obtained, each sample was processed, embedded in paraffin , then cut 3-5 µ thick and stained with Hematoxylin & Eosin and Masson trichrom. Other slides were prepared on charged slides for immune-histochemistry. Diagnosis of CC is based on prescence of thicknening of the subepithelial collagenous band to more than 10 µm, infilteration of lamina propria with inflammatory cells, increased intraepithelial lymphocytes and may be surface epithelial injury. If more than 20 intraepithelial lymphocytes per 100 epithelial cells with normal collagen band is present, diagnosis of LC is confirmed.

2.4. Statistical Analysis

Statistical analysis was done by using IBM-SPSS software version 21, four windows.

2.5 Ehics

The Approval by Mansoura medical ethics Committee (MMEC) of faculty of medicine was obtained and written consents from patients participated in the study or from their family were also obtained.

3. Results

Our study included 120 patient with IBS-D, 50(41.6%) males and 70(58.3%) females with a mean age 43.16±15.21 year. After doing Colonscopy, distinct organic diseases were found in 19 patient and those patients were excluded (Table 1). Colonscopy were completely free in 101 patient and previous diagnosis of IBS was setteled. Three samples from the normal mucosa of each colonic segment were obtained and sent for histopathological examination.

In 90 (89.1%) of those patients histopathological examination of colonic biopsies were completely normal confirming prescence of IBS. MC was found in 11(10.8%) of cases. Of those 11 cases, 9(8.9%) diagnosed with LC and 2 (1.9%) cases with CC.

In our study, women are affected with MC more than men, 7 from 11 case were womens with a mean age of 49.15 ± 11.23 years (Table 2). MC was found to be more common in smokers, 6 (54. 5%) of cases of MC were found to be smokers (Table 2).

In the present study, diarrhea was the main presenting symptom of patients with MC, 9 (81.8%) of cases present with diarrhea that was associated with nocturnal attacks in 8 (72.7%) of cases with a mean frequency 4 times per day. History of previous recurrent gastroentritis, was found in 2 (18.1%) cases and history of drug intake in 6 (54.5%) Cases (Table 2). Among 11 patients with MC, we found that 5 (45.4%) of patients associated with autoimmune diseases, 4 cases with type 1 DM and one case with hypothyoridism (Table 2).

On histopathological examination of colonic biopsies, features of LC (Figure 1) was found 9 (81.8%) and CC (Figure 1) in 2 (18.18%) of patients with MC. In our study, 8 (72.7%) of biopsies diagnosed with MC were obtained from rectosigmoid and left side of the colon while the remaining obtained from the ascending colon.

Table 1: Colonscopic findings in the studied group

Colonscopy	*Number*	*%*
Completely free	101	84.16
Diverticular disease	5	0.04
Inflammatory bowel disease	6	0.09
Colorectal cancer	1	0.008
Non specific colitis	7	0.058

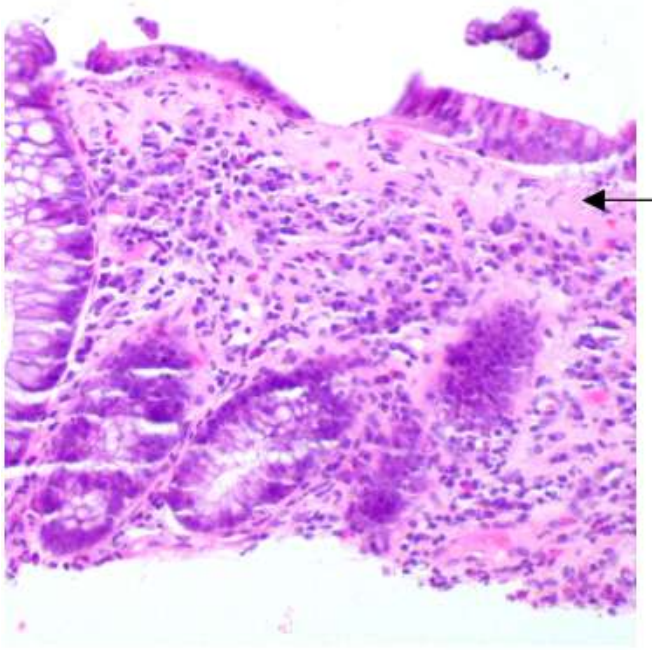

Figure 1 : collagenous colitis with thickened subepithelial band

Table 2: Clinical features of the studied group

	Microscopic colitis (n = 11)	IBS-D (n = 90)	*P*
Age	49.15 ± 11.23	39.26 ± 13.29	P = 0.005
Sex			
Male	4 (36. 3%)	41 (45. 5%)	P = 0.071
Female	7 (63.6%)	49 (54. 4%)	P = 0.032
Smoking	6 (54. 5%)	34 (37. 7%)	P = 0.041
Symptoms			
Diarrhea	9 (81.8%)	60 (66. 6%)	P = 0.044
Nocturnal attacks	8 (72.7%)	12 (13. 3%)	P < 0.0001
Abdominal pain	3 (27. 2%)	55 (61. 1%)	P = 0.0222
Flatulence	1 (0. 09%)	59 (65. 5%)	P = 0.0005
Weight loss	7 (63.6%)	10 (11. 1%)	P = 0.0005

History of recurrent gastroentritis	2 (18.1%)	49 (54.4%)	P = 0.0019
History of drug intake	6 (54. 5%)	33 (36. 6%)	P = 0.039
Associated diseases	5 (45.4%)	20 (22. 2%)	P = 0.0311

4. Discussion

Diarrhea-predominant IBS is relatively a common gut disease, but due to absence of pathognomonic diagnostic features and specific diagnostic tools it can be easily misdiagnosed. Apart from inflammatory bowel diseases as the most frequent cause of chronic diarrhea, a number of poorly known diseases can still remain misdiagnosed and treated under the assumption of an IBS (8).

In the past, MC was considered to be a rare condition with very little knowledge available about its etiology or epidemiology. Now It has become apparent that MC is regarded as common cause of chronic diarrhea in middle-aged and elderly patients (9).

In our study, MC was detected in 10.8% of patients presented by chonic diarrhea, of those 8.9% with LC and 1.9% with CC with a mean age of diagnosis of 49 year. This was in agreement with a study carried out by **Olesen et al** who found that MC was detected in 10% of the colonoscopic biopsies from patients with chronic watery diarrhea but CC were detected in 5% and LC in 4.5% of patients (10). Another study by **Tuncer et al** reported an incidence of LC of 23.5% patients previously diagnosed with IBS (11). This differrence may be due to the small number of patients diagnosed with MC based on histopathological criteria.

Actually, it is difficult to determine exactly the epidemiology of MC due to two causes. First, the low specificity of symptoms and signs may cause the diagnosis to be missed or at least delayed. Secondly, there were no epidemiological population based studies where the scientific literature on MC mainly consisting of sporadic case reports. It is therefore unclear whether the increased incidence of MC is real or a simple consequence of the increased attention about the disease (12).

In the present study, females are more affected with MC where 63.6% of cases diagnosed with MC were females.There is statisticaly significant higher expression of MC in smokers in comparison with D-IBS with $P < 0.005$ (Table 2). Associated autoimmune diseases were significantly detected in MC with $P < 0.05$ (Table 2). From these data it appears that higher age, female gender, smoking and prescence of concomitant autoimmune diseases are risk factors for MC.

This is in agreement with **Agnarsdottir et al** and **Olesen et al** who investigated risk factors for MC and concluded that advanced age, female gender, prescence of associated autoimmune diseases such as thyroid disease or celiac disease are risk factors for MC (13,14). This age distribution is unexplained and may be biased because colonoscopies with or without biopsies is not pronounced in younger patients without alarm symptoms and this may be responsible for underestimation of incidences rates of MC in younger populations. Gender differrence may be due to possible role of hormonal alterations or an ascertainment bias in women remain speculative (15).

In our study, MC was significantly linked with the use of NSAIDs as 54.5% of patients diagnosed with MC were using NSAIDs. **Capurso et al** found a link between MC and the consumption of some drugs especially NSAIDs, proton pump inhibitors (Lansoprazole) and ticlopidine (16). The difference between our study and this study may be due to relatively small number of cases in our study and we stressed also on NSAIDs due to the common use in our community especially in old age.

Diarrhea was the main presentation of patients diagnosed with MC in our study, it was associated with nocturnal attacks in 72.7% of cases with a mean frequency 4 times per day. This runs paralel to **Abboud et al** who showed that in contrast to IBS, patients with MC can present with nocturnal diarrhea, arthralgias and fecal incontinence (17). **Stoicescu et al** concluded that clinical picture is insufficient in differentiating patients with IBS from patients with MC (18). **Limsui et al** found that approximately one half of patients with MC met the symptom based criteria for IBS. It is therefore not surprising that there is symptomatic overlap between these two entities. They recommend that patients with IBS-D should undergo colonoscopy to exclude MC (19).

Rahman et al also reported that there is a considerable overlap in symptoms between the patients of IBS-D and patients with MC. Without colonoscopy and biopsy from multiple sites, possibility of MC cannot be excluded in patients with IBS-D and it can be asumed that clinical symptom based criteria for IBS are not sufficient enough to rule out the diagnosis of MC (20).

5. Conclusion

We concluded that, MC is not uncommon disease in Egypt that commonly missed in patients with IBS-D. The dependence on clinical presentation alone is insufficient in differentiation between them where the corner stone of diagnosis is histopathological features. So, there must be strict coordination between the clinician and the pathologist where the pathologist should receive a full clinical data and representative biopsy. Large scale multicenter studies are needed to clarify exactly the prevalence of MC in Egypt.

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