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Microscopic Colitis: A Report of 20 Cases and Review of the Literature

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ABSTRACT

Microscopic colitis, including lymphocytic colitis (CL) and collagenous colitis (CC), is a chronic inflammation of the colon accompanied by non-bloody aqueous diarrhea, while the colonic mucosa has a normal or almost normal macroscopic appearance. It is a benign affection that can evolve spontaneously towards remission or, more often, evolve with phases of respite and relapse. The physical examination is strictly normal and laboratory tests do not reveal any anomalies. The diagnosis will be confirmed by colonic biopsies staged per-colonoscopy. CL is characterized by an increase in intraepithelial lymphocytes, while CC is characterized by a thickening of the subepithelial collagen band. In the light of data from the literature, we will study the epidemiological, clinical, endoscopic and histological characteristics of microscopic colitis through a series of 20 cases collected in the Medical Clinic B of IbnSina University Hospital in Rabat.

Introduction

Microscopic colitis is defined by the association of watery non-bloody-diarrhea, macroscopically normal or near normal appearance of the colonic mucosa, and microscopic inflammation of the colon.

Microscopic colitis include collagen colitis CC which is characterized by the existence of a thickening of the subepithelial collagen bandand lymphocytic colitis LC characterized by an increase in lymphocytes intra Epithelial.

The objective of this work is to specify the epidemiological, clinical, evolutionary and therapeutic characteristics of these affections through a series of 20 cases (13 cases of colitis collagen and 7 cases of lymphocytic colitis).

Materials and Methods

This is a retrospective study of 18 cases of microscopic colitis collected at the Medical Clinic B of IbnSina University Hospital in Rabat, Morocco.

Inclusion criteria were chronic watery diarrhea, normal colonic endoscopic appearance, colonic epithelial collagen greater than 10 µm on histologic examination for CC, and epithelial hyperlymphocytosis > 30% for the LC.

The following elements were evaluated: age, sex, taking drugs that can trigger these colitis (PPIs, NSAIDs, statins...), smoking concept, gastrointestinal and extra digestive manifestations.

All patients undergo a biological assessment (NFS, ionogram, TSH, coproparasitology of stool), ileocoloscopy with staged colon biopsies.

Results

Our study concerns 20 cases of microscopic colitis collected over a period of 15 years. These include 13 cases of collagen colitis (60%) and 7 cases of lymphocytic colitis (40%). The average age of the patients is 47 years with extremes ranging from 21 to 73. There is a clear predominance of women (14 women and 6 men).

Clinically, diarrhea was the reason of hospitalization for all patients. It was aqueous, non-bloody and intermittent with a variable frequency of 3 to 12 stools / day. It evolved between 2 months and 6 years before diagnosis with an average of 3 years. Other gastrointestinal manifestations were abdominal pain in 7 cases (38.9%), abdominal ballooning in 5 cases (27.8%) and vomiting in 2 cases (11%). Extradigestive manifestations were represented by anemic syndrome in 6 cases (33.3%), slimming in 4 patients (22.2%) and polyarthritis in 3 cases (16.7%).

Biologically, anemia was observed in 6 cases (33.3%), an inflammatory syndrome is noted in 5 cases (27.8%), hypoalbuminemia in 3 cases (16.7%) and hypokalemia in one case (5.6%).

At the endoscopic level, the appearance of the colonic mucosa was normal. Serial biopsies of the colon were performed in all patients. Histological examination showed a subepithelial collagen band thicker than 10um in 13 cases (61%) and increased the number of intraepithelial lymphocytes (IEL) to 20 or more per 100 surface epithelial cells in the other 7 patients (39%).

The treatment consisted of the prescription of Anti-diarrheal medications "Loperamide" in all patients. This treatment was effective only in 8 patients (33.3%). Salicylates were prescribed for 10 patients (55.6%) with a marked improvement for half of them. We used the prescription of corticosteroids in 2 cases (11%) with a good evolution.

Discussion

Microscopic colitis brings together two main entities: collagen colitis and lymphocytic colitis. It is an anatomoclinic syndrome characterized by the association of chronic watery diarrhea, normal endoscopic appearance and histological abnormalities [1].CL is characterized by an increase in intraepithelial lymphocytes greater than 20% of the cells, whereas CC is characterized by a thickening of the subepithelial collagen band greater than 10 µm [2].

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MC is a rare disease that has increased in incidence from 10% to 20% since colorectal biopsies have been used in the investigation of chronic diarrhea [3]. The prevalence of CM is 1/1000. The annual incidence (4-18 per 100,000 / year) is increasing [4]. A recent French study reported that the incidence of MC was 7.9 per 100,000 inhabitants, similar to the incidence of Crohn's disease in that population [5]. Numerous studies have highlighted the predominance of women as in our series (14 women and 6 men) [4,6].The mean age at diagnosis is estimated to be between 60 and 70 years of age, but MC has been described in all age groups, including the pediatric population [7, 8]. In our series, the average age of our patients is 47 years old.

The etiology of MC remains unknown. Genetic origin is unlikely. However, family cases have been reported [9]. Analyzes of colonic biopsies have demonstrated an increase in mucous permeability favoring invasion of the mucosa by microbes of the digestive flora [10]. CM is associated with certain medications such as nonsteroidal anti-inflammatory drugs (NSAIDs), proton pump inhibitors (PPIs), and serotonin reuptake inhibitors (SSRIs). Nevertheless, no causal link has yet been demonstrated [11]. Some studies suggest that malabsorption of bile acids may be a causative factor [12]; others suggest that smoking is a risk factor for MC [13, 14].The pathophysiology has been well studied: inflammation induces a decrease in the resorption of potassium and chlorides, moreover, there is an active secretion of chlorides. The epithelial barrier is impaired with a dysfunction of tight junction. Thus, the liquid fraction of the stool is increased, causing diarrhea [15].

Clinically, chronic non-bloody watery diarrhea is the main symptom of MC. The frequency of stool can vary greatly depending on the severity of the disease (3-20 times per day). In our study, stool frequency was variable from 3 to 12 stools per day. Diarrhea usually occurs daily, sometimes intermittent and often nocturnal. It may be accompanied by abdominal pain, faecal incontinence, weight loss and asthenia [16,17]. MC is rarely associated with serious complications, however, cases of spontaneous perforation and post-colonoscopy have been reported [18, 19]. There is an association between CM and certain autoimmune diseases such as celiac disease, thyroid diseases, rheumatoid arthritis and type 1 diabetes [20]. Indeed, a recent Canadian study has shown a strong association between CM and celiac disease [21]. This highlights the particular importance of colon biopsy in dealing with celiac disease resistant to a well-conducted gluten-free diet. Conversely, in case of unfavorable progression of CM under treatment, celiac disease must be sought.

The diagnosis of CM is based on the combination of a classic clinical presentation (chronic diarrhea) and endoscopic and histological confirmation. The biological assessment is usually normal; lactoferrin and fecal calprotectin, which can be used as non-invasive markers of inflammation in ulcerative colitis and Crohn's disease, are of no contribution to the diagnosis of CM [22]. Classically, the macroscopic appearance of the colonic mucosa is normal.This is the case of all our patients (Figure 1). Nevertheless, minor abnormalities such as erythema and edema have been described [23, 24].

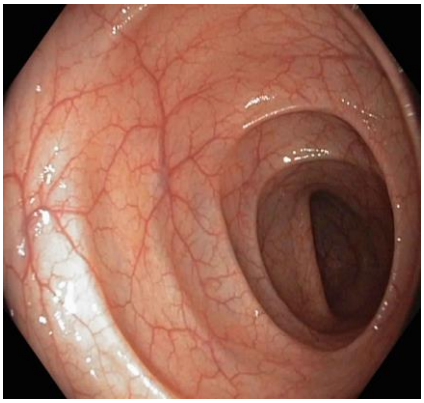

Figure 1. Colonic mucosa with normal endoscopic appearance.

Histologic hallmarks of disease in macroscopically unremarkable colon form the diagnostic cornerstone in MC. There are two constant and common histological diagnostic criteria for both types of CM (CC and CL): the alteration of the surface epithelium and the inflammatory infiltrate of the lamina propria by lympho-plasmocytes mixed with neutrophils and eosinophils. However, CL is characterized by the presence of epithelial hyperlymphocytosis, which often reaches 30 to 40% (N <5%) (Figure 2), knowing that a less marked hyperlymphocytosis (about 20%) is frequent in CC patients whose positive diagnosis is based on the presence of a net thickening (> 10 µ) of the subepithelial collagen band (N <7µ) [25] (Figure 3). In most cases, the entire colon is affected. Nevertheless, there are sometimes a rectal and sigmoidal savings. Rectosigmoidoscopy is then not sufficient to make the diagnosis. Very rarely, extracolic involvement (gastritis, duodenitis, ileitis) has been described [25].

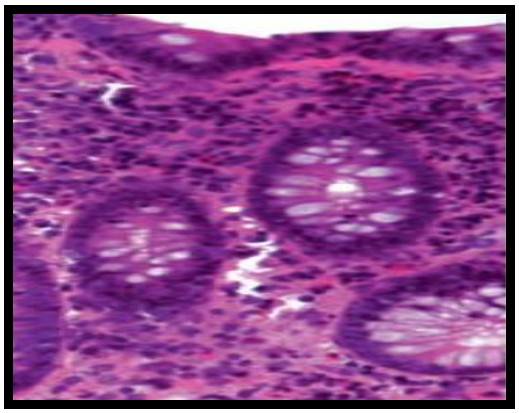

Figure 2. Lymphocyte colitis: note the increased numbers ofintraepithelial lymphocytes.

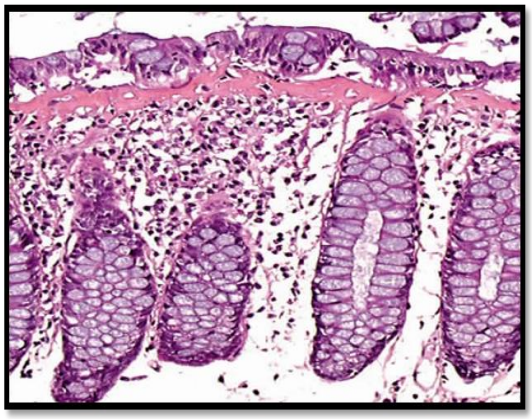

Figure 3. Collagenous colitis: net thickening (> 10 µ) of the subepithelial collagen band.

The therapeutic choice will take into account the severity of the symptoms as well as the quality of life of the patient. No curative treatment currently exists for CM. The goal of the therapy is to induce clinical remission with a better subsequent quality of life [26]. Stopping smoking is recommended as well as stopping medications that may cause CM. Generally, most patients have already received symptomatic antidiarrheal treatment such as loperamide, which may sometimes have some clinical benefit. Such treatment is of course not effective on inflammation. It is therefore not surprising that the effect is only transient. On the other hand, anti-inflammatory treatment with steroidal glucocorticoids has been shown to be effective in different studies. In order to avoid the side effects associated with such repeated systemic or long-term treatment, budesonide has been used successfully in many studies [27,28]. Nevertheless, 60 to 80% of patients will relapse a few weeks after stopping the treatment. This risk is correlated with the duration and severity of the disease. In these cases, a second therapeutic attempt with budesonide at 9 mg / day, followed by a dosage reduced to 6 mg / day for a period of six months, is effective in about 70% of cases. Further reduction of the dosage is possible. Other anti-inflammatory therapies, which have been shown to be effective in IBDs, such as mesalazine, azathioprine or 6-mercaptopurine, methotrexate, and anti-TNF, are also promising in CM. However, further studies are needed for a recommendation of these treatments. Other treatments have been used such as probiotics, cholestyramine, bismuth salicylate [29]. Surgical intervention by subtotal colectomy and ileostomy may be necessary in very severe cases not responding to conventional drug treatments. In our series, the treatment consisted of the prescription of standard antidiarrheal agents, in all patients with a clear efficiency in 8 patients. Salicylates were prescribed for 10 patients and corticosteroids in 2 cases with good evolution.

A simplified algorithm for the therapeutic management of CM has been proposed by Munch A. et al [16] (Figure 4).

Although CM can be very debilitating, it is a mild disease with no increased risk of cancer [30]. Endoscopic monitoring is therefore not necessary. On the other hand, clinical follow-up of patients with CM is necessary [31].

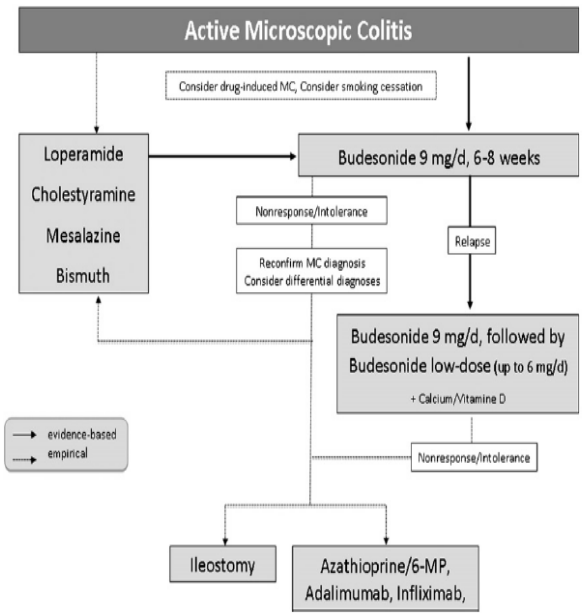

Figure 4. Treatment algorithm for active microscopic colitis.

Conclusion

Our study emphasizes the importance of biopsies in case of chronic diarrhea with normal endoscopy. Microscopic colitis is not uncommon during chronic diarrhea. Its etiopathogenesis remains poorly known. Careful histories are recommended to identify possible triggers, especially in patients taking multiple medications for comorbidities. The usual benignity of microscopic colitis justifies drug treatment according to a progressive strategy. The introduction of budesonide has revolutionized the treatment of CM. The evolution is often favorable under adapted treatment. Recurrence is not uncommon, and patients should be monitored clinically.

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