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Lansoprazole Associated Lymphocytic Colitis With Irritable Bowel Syndrome in a Patient Without Symptoms of Diarrhea

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Abstract

We present a case of 64-year-old woman patient who developed microscopic colitis undergoing lansoprazole therapy for gastroesophageal reflux disease. Abdominal pain and mild weight loss had been developed. She had no symptoms of diarrhea. Appearance on colonoscopy was normal, but biopsies showed lymphocytic colitis. Lansoprazole therapy was ceased. A repeat colonoscopy 2 months after discontinuation revealed endoscopic and histological normalization.

Keywords: Microscopic colitis; Lansoprazole; Gastroesophageal reflux disease

Introduction

Microscopic colitis (MC) is characterized, clinically, by chronic or recurrent watery diarrhea without bleeding. There are well-defined histological findings and normal or nearly normal macroscopic findings on colonoscopy [1]. Collagenous colitis (CC) and lymphocytic colitis (LC) are the two major histological forms of MC. They have nearly the same clinical and macroscopical colonic mucosal findings [2, 3]. Pathogenesis of MC is unknown [4, 5]. The most widely postulated hypothesis is, the inflammatory disorders arising from epithelial immune responses to intraluminal dietary or bacterial contents, environmental risk factors such as drugs, have been suggested as a cause of this process, include non-steroidal anti-inflammatory drugs, simvastatin, selective seratonin reuptake inhibitors, acarbose, biphosphonates and proton pump inhibitors (PPIs) [6-9]. We report a case of lansoprazole-associated LC with a constipation dominant irritable bowel syndrome (IBS) as a concomitant disease.

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Case Report

A 64-year-old woman with abdominal pain and mild weight loss was referred to a gastroenterologist. The patient fulfilled ROME III criteria. She presented a history of abdominal discomfort associated with improvement with defecation, constipation, bloating and gas for about 20 years but more frequent for the past 4 - 5 years. The patient reported receiving PO lansoprazole 30 mg/day to treat gastroesophageal reflux disease for nearly 1 month. The medical history report also revealed that the patient was not receiving any concomitant medications or treatments at the time. After listening to the story of the patient and physical examination, complete blood count, erythrocyte sedimentation rate and biochemical tests were performed. An abdominal mass, hepatomegaly, fever, arthritis, dermatitis or signs of malabsorption were not found on physical examination; there were not abnormalities on initial laboratory tests including anemia, thyroid dysfunction, increased sedimentation rate, leukocytosis, presence of occult blood in stool or other abnormal biochemical findings. The patient had negative results on serological tests for coeliac disease (transglutaminase and endomysial antibody) and normal serum IgA levels. In pa-

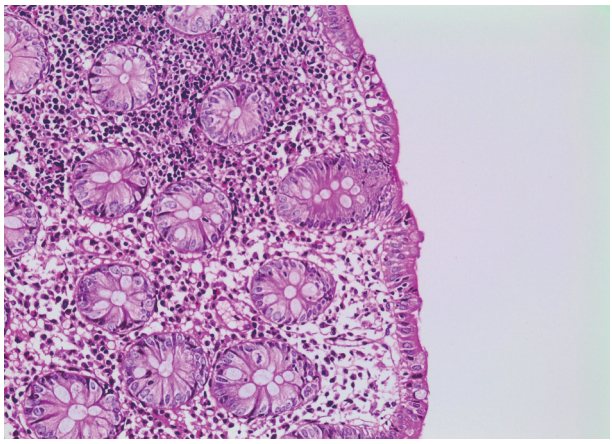

Figure 1. There are intraepithelial lymphocytosis and increased level of lymphoplasmositer cells in the lamina propria (H&E, × 200).

tient with the alarm signs such as weight loss, advanced age of onset, family history (cancer), colonoscopy was done. Appearance on colonoscopy was normal, but biopsies showed LC (Fig. 1). Lansoprazole therapy was ceased. Eight weeks later, endoscopic and histological normalization was ascertained.

Discussion

MC is regarded as a common cause of chronic watery diarrhea, accounting for approximately 4-13% of patients presenting with this symptoms [10]. LC and CC are the two major subtypes of MC with increasing prevalence of 10 - 15.7/100,000 and 14.4/100,000 [10-13]. Increased awareness of the disease among clinicians and increased use of several drugs that cause MC are some of the causes of more frequent diagnosis. Since the growing incidence of MC seems to parallel the rise in the use of PPIs, it is essential to understand the association between MC and PPIs. A recent study from Netherlands found that 11.8% of the population had at least one prescription for PPIs in 1 year [14].

Initially, lansoprazole has been found to be associated with MC [8]. The frequency of lansoprazole-associated MC is unknown, at least 0.7% was found to develop MC [15]. There are several studies which further highlight the association between the PPIs and MC. Most common mechanisms are inhibition of colonic proton pumps which affect the local electrolyte balance, induction of smooth muscle relaxation that inhibit contractile activity, increased paracellular permeability and alteration of intestinal microbial flora [16-18].

Almost all the studies lansoprazole associated with MC are mentioning the watery diarrhea and normal or nearly normal macroscopic colonic mucosa. There are some studies designed as a retrospective analysis of colonic biopsies show that LC or CC were not confined to the patients just with diarrhea as a presenting symptom, but were also present with normal bowel movements and constipation. Wang et al mentioned 12 patients fulfilled the histological criteria but not the clinical criteria for classic LC and classified them as having atypical LC [19]. Nooroudien et al retrospectively reviewed non-malignant colon mucosal biopsies with 20 cases of LC, and mentioned the most common presenting complaints of them were chronic diarrhea in 9/20 cases, abdominal pain in 7/20 and constipation in 3/20 [1]. Neal et al studied clinicopathological association and prevalence of LC in 100 asymptomatic, non-gluten sensitive adults who underwent screening surveillance colonoscopy for previous colonic polyps as a control group without a clinical symptom, and none had abdominal pain, weight loss or altered bowel habits. Of the 100 asymptomatic patients 4% had classic LC with no clinical symptoms [20]. One recent study to investigate the incidence of LC in patients with Hashimoto's thyroiditis found that 20 of 50 patients had LC. Only five of the patients had diarrhea; the other 15 patients were asymptomatic. In a recent study, Yeon et al reviewed patients' histological reports receiving PPIs who had no symptoms of diarrhea and matched the controls. The intraepithelial lymphocyte count was significantly higher in the PPI group than controls. They suggested the findings as an early stage of the disease even before the onset of the symptoms [21].

In a large retrospective study, celiac disease, IBS and thyroid diseases were found to have a higher occurrence in MC compared to controls [22]. The symptomatic overlap between IBS and microscopic colitis makes the diseases difficult to be diagnosed clinically and suggests that a colonoscopy is imperative [23]. Almost all the studies, which were trying to show the association of MC and IBS were made with patients who have diarrhea predominant IBS (IBS-D) [24-26]. In a recent study patients previously diagnosed as IBS reported 6.07% MC with 5.27% of LC and 0.8% of CC. While other authors found the incidence of CC 7.2% and LC 2.2 % among the patients diagnosed as IBS [25, 27]. There are few reports about the constipation predominant IBS and MC. Carmona-Sanchez et al reviewed 155 patients with IBS-D and 145 with IBS-C. Both groups were matched from the standpoint of age, gender ratio and time course of disease. MC was detected in 28 patients with IBS-D and in one with IBS-C (18% vs. 0.7%, $P < 0.0001$) [28].

Our case illustrates a rare condition of MC, without any symptoms of diarrhea and concomitant with constipation dominant IBS. Although lansoprazole is a widely prescribed drug for gastroesophageal reflux and peptic ulcer disease, the frequency of lansoprazole-associated MC is not well-estimated for subjects without symptoms of diarrhea. We think that the incidence of lansoprazole-associated MC is higher than known incidence.

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