Lansoprazole-associated collagenous colitis: Diffuse mucosal cloudiness mimicking ulcerative colitis

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INTRODUCTION

Collagenous colitis and lymphocytic colitis, collectively termed microscopic colitis, are considered to be etiologically related and to be a spectrum of the same disease. The disease is well known to have normal mucosa endoscopically. However, endoscopic abnormalities are observed in about 30% of cases: abnormal vascular pattern, loss of vascular pattern, edema, and erythema. The treatment of the disease is similar to that in ulcerative colitis. The etiology of the disease is unknown but a significant proportion may be drug-induced. Immunological disposition is implicated because the disease is often seen in patients with a variety of autoimmune diseases.

Lansoprazole is widely prescribed for gastroesophageal reflux and benign peptic ulcer disease. We present a case of lansoprazole-associated collagenous colitis where the mucosa showed diffuse cloudiness mimicking ulcerative colitis. We mistook this case initially for an atypical case of ulcerative colitis. Withdrawal of lansoprazole promptly resolved the diarrhea. Endoscopic and histological abnormalities were also completely resolved, similar to the first episode. Retrospectively, the date of commencement of sulfasalazine and discontinuation of lansoprazole in the first episode was found to be the same. We conclude that this patient had lansoprazole-associated collagenous colitis.
of ulcerative colitis, and the patient was then diagnosed with collagenous colitis, which seemed to respond to sulfasalazine. In fact, the response was to the removal of lansoprazole.

CASE REPORT

A 70-year-old woman with watery diarrhea four to nine times a day in an orthopedic ward was referred to a gastroenterologist at the beginning of April 2007. She had a past history of: pulmonary tuberculosis and hypertension at 54 years, cerebral hemorrhage with a sequel of left hemiplegia at 63; diabetes mellitus, constipation, internal hemorrhoid and interstitial pneumonia at 67; neurogenic bladder at 68; gastroduodenal ulcers at 69; and reflex esophagitis at 70. She had a fracture of the femoral head and underwent surgery for insertion of an artificial femoral head on March 16, 2007. The patient had diarrhea four to nine times a day since March 26. Abnormalities on routine blood testing included mild anemia (hemoglobin 105 g/L), hypoproteinemia (49 g/L) and increased C-reactive protein (33 mg/L). Stool culture for pathogens was negative and fecal occult blood tests were negative. The following immunological and hormonal tests were normal: anti-nuclear antibody, rheumatic factor, perinuclear antineutrophil cytoplasmic antibody, anti-Scl 70 antibody, anti-centromere antibody, thyroid test, microscopy antibody, free T3, free T4, and thyroid stimulating hormone. The gastroenterologist (MC) decided to check her drugs for diarrhea as a side effect and asked the orthopedist to withdraw lansoprazole 30 mg/d if possible, and to change loxoprofen sodium to etodolac. Lansoprazole had been prescribed for reflux esophagitis for nearly 6 mo and loxoprofen sodium had been prescribed for anal pain of unknown cause after the episode of diarrhea. Neither metronidazole of 1 wk duration for suspected antibiotic-associated diarrhea nor trimethoprim maleate of 1 wk duration for suspected irritable bowel syndrome was effective. Therefore, colonoscopy was performed on April 16. This disclosed diffuse cloudiness of the mucosa in the entire colorectum observed from the rectum to the descending colon (Figure 1A). These findings suggested ulcerative colitis. Consequently, sulfasalazine 2 g/d was started that day. The patient’s diarrhea dramatically disappeared on the following day. The findings of three biopsy specimens each from the descending colon, the sigmoid colon, and the rectum showed similar results: erosion and moderate infiltration of inflammatory cells were observed: red spots [13], mucosal tears [15, 16], hemorrhagic lacerations [17], and longitudinal ulcers [18]. In our case, distinct diffuse cloudiness of the mucosa was observed on two occasions in this patient with collagenous colitis. In collagenous colitis, in addition to subepithelial collagenous thickening, there are significant numbers of inflammatory cells in the lamina propria. These changes completely disappear on recovery. Therefore, it seems reasonable that diffuse mucosal cloudiness rather than normal mucosa is endoscopically observed in collagenous colitis.

Microscopic colitis was originally described as mucosa that is endoscopically normal. Recently new endoscopic findings have been added: red spots [19], aphthoid ulcer [20], ulcer [21], mucosal tears [15, 16], hemorrhagic lacerations [17], and longitudinal ulcers [18]. In our case, distinct diffuse cloudiness of the mucosa was observed on two occasions in this patient with collagenous colitis. In collagenous colitis, in addition to subepithelial collagenous thickening, there are significant numbers of inflammatory cells in the lamina propria. These changes completely disappear on recovery. Therefore, it seems reasonable that diffuse mucosal cloudiness rather than normal mucosa is endoscopically observed in collagenous colitis.

Microscopic colitis is associated with a variety of immunological disorders and immunological phenomena: thyroid disease, rheumatoid arthritis, polyarthritis, CREST syndrome, eosinophilia, and the presence of autoantibodies [22, 23]. The present case had interstitial pneumonia, which is frequently associated with autoimmune diseases. Interstitial pneumonia is to be added to a list of immunological disorders associated with microscopic colitis.

Microscopic colitis is known to be associated with various drugs including nonsteroidal anti-inflammatory drugs [24]. Recently, lansoprazole has been shown to cause microscopic colitis [9-12, 18]. The frequency of lansoprazole-associated microscopic colitis is not known, but at least six of 850 subjects who took lansoprazole (0.7%) were found to develop microscopic colitis [24]. The period from
Initiation of lansoprazole to the onset of diarrhea varies extensively from 5 d to 9 mo [9-12]. In our case, it was about 3 and 6 mo in the two episodes, respectively. Treatment of lansoprazole-associated microscopic colitis is withdrawal of lansoprazole. Prompt resolution of diarrhea occurs within 1-10 d [9-12]. In our case, it was 1 d in the first episode and a few days in the second episode. Complete histological normalization subsequently occurred in our case [10,11]. In lansoprazole-associated microscopic colitis, the substitution of omeprazole for lansoprazole was reported to be successful without diarrhea [10].

From the present case it can be concluded that: diffuse cloudiness of colorectal mucosa can be seen endoscopically in collagenous colitis; lansoprazole can cause microscopic colitis; and discontinuation of lansoprazole results in the prompt resolution of diarrhea.

REFERENCES

1 Veress B, Löfberg R, Bergman L. Microscopic colitis syndrome. Gut 1995; 36: 880-886
2 Pimentel RR, Achkar E, Bedford R. Collagenous colitis. A treatable disease with an elusive diagnosis. Dig Dis Sci 1995; 40: 1400-1404
3 Bohr J, Tysk C, Eriksson S, Abrahamsson H, Järnerot G. Collagenous colitis: a retrospective study of clinical presentation and treatment in 163 patients. Gut 1996; 39: 846-851
4 Zins BJ, Sandborn WJ, Tremaine WJ. Collagenous and lymphocytic colitis: subject review and therapeutic alternatives. Am J Gastroenterol 1995; 90: 1394-1400
5 Riddell RH, Tanaka M, Mazzoleni G. Non-steroidal anti-inflammatory drugs as a possible cause of collagenous colitis: a case-control study. Gut 1992; 33: 683-686
6 Kakar S, Pardi DS, Burgart LJ. Colonic ulcers accompanying collagenous colitis: implication of nonsteroidal anti-inflammatory drugs. Am J Gastroenterol 2003; 98: 1834-1837

Figure 1 Colonoscopy on April 16 (A) and May 17 (B), 2007 showed diffuse cloudiness of mucosa in the colon and clear normal vascular patterns, respectively.

Figure 2 Biopsy specimens taken on April 16 (A) and May 17 (B), 2007 (hematoxylin and eosin staining, × 100). The former showed erosion, moderate infiltration of inflammatory cells in the lamina propria, and subepithelial collagenous thickening. The latter showed disappearance of these abnormalities.

Figure 3 Biopsy specimens taken on April 16 (A) and May 17 (B), 2007 (Masson’s trichrome staining, × 200). Subepithelial collagenous thickening (A, arrows) disappeared on May 17 (B).
7 Berrebi D, Sautet A, Flejou JF, Dauge MC, Peuchmaur M, Potet F. Ticlopidine induced colitis: a histopathological study including apoptosis. J Clin Pathol 1998; 51: 280-283
8 Roubenoff R, Ratain J, Giardiello F, Hochberg M, Bias W, Lazenby A, Yardley J. Collagenous colitis, enteropathic arthritis, and autoimmune diseases: results of a patient survey. J Rheumatol 1989; 16: 1229-1232
9 Wilcox GM, Mattia A. Collagenous colitis associated with lansoprazole. J Clin Gastroenterol 2002; 34: 164-166
10 Thomson RD, Lestina LS, Bensen SP, Toor A, Maheshwari Y, Ratcliffe NR. Lansoprazole-associated microscopic colitis: a case series. Am J Gastroenterol 2002; 97: 2908-2913
11 Rammer M, Kirchgatterer A, Hobl King W, Knoflach P. Lansoprazole-associated collagenous colitis: a case report. Z Gastroenterol 2005; 43: 657-660
12 Hilmer SN, Heap TR, Eckstein RP, Lauer CS, Shenfield GM. Microscopic colitis associated with exposure to lansoprazole. Med J Aust 2006; 184: 185-186
13 Katsinelos P, Katsos I, Patsiaoura K, Xiarchos P, Goulis I, Eugenidis N. A new endoscopic appearance of collagenous colitis. Endoscopy 1997; 29: 135
14 Yabe M, Igarashi K, Hata K, Ho N, Tsukioka S, Shibuya H. A case of collagenous colitis with a unique endoscopic appearance. Gastroenterol Endosc 1997; 39: 1099-1104
15 Cruz-Correa M, Milligan F, Giardiello FM, Bayless TM, Torbenson M, Yardley JH, Jackson FW, Wilson Jackson F. Collagenous colitis with mucosal tears on endoscopic insufflation: a unique presentation. Gut 2002; 51: 600
16 Wickbom A, Lindqvist M, Bohr J, Ung KA, Bergman J, Eriksson S, Tysk C. Colonic mucosal tears in collagenous colitis. Scand J Gastroenterol 2006; 41: 726-729
17 Richieri JP, Bonneau HP, Cano N, Di Costanzo J, Martin J. Collagenous colitis: an unusual endoscopic appearance. Gastrointest Endosc 1993; 39: 192-194
18 Watanabe T, Hirakawa K, Sato S, Kochi S, Nakajima Y, Aoyagi K, Matsumoto T, Iida M. A case with collagenous colitis and multiple longitudinal ulcers. Gastroenterol Endosc 2008; 50: 27-33

S- Editor Li LF  L- Editor Webster JR  E- Editor Zheng XM