Collagenous Colitis Associated with Rabeprazole in a Peritoneal Dialysis Patient

Collagenous colitis is a disease causing chronic watery diarrhea, which is histologically accompanied by thickening of the subepithelial collagen layer (1). Although the exact cause of collagenous colitis is unknown, frequent use of proton pump inhibitors (PPIs) in clinical practice appears as one cause reported from around the world (2,3). Collagenous colitis due to use of PPIs in hemodialysis (HD) patients has recently been reported in some cases in Japan; however, there are few reports of collagenous colitis in peritoneal dialysis (PD). We report herein a case of collagenous colitis due to rabeprazole in a PD patient.

CASE DESCRIPTION

A 74-year-old man with a history of ischemic heart disease, right renal cell carcinoma, and early-stage gastric carcinoma started PD because of end-stage kidney disease resulting from nephrosclerosis. He was admitted with cerebral infarction at 5 months after the introduction of PD. He developed watery diarrhea once a day during the hospitalization. Although he had suffered from watery diarrhea before discharge, the clinical course had been observed without treatment. Watery diarrhea continued three times a day. An antifatulent (Biofermin® 3.0 g/day; Biofermin, Kobe, Japan) was prescribed for watery diarrhea in the PD outpatient department 1 month later. However, symptoms did not subside, and, after his weight fell by 3 kg in 1 month, he was finally admitted to our hospital. He had no history of overseas travel and no contact with people who complained of diarrhea. Furthermore, he had not developed PD-associated peritonitis in the past, was not taking antibiotics for more than half a year, and had not recognized any preceding symptoms of the common cold. He had been taking amlodipine (10 mg/day), bisoprolol (5 mg/day), and carvedilol (20 mg/day) to treat hypertension, and warfarin (2.5 mg/day) and clopidogrel (75 mg/day) to treat ischemic heart disease and lacunar infarction for

several years. In addition, the PPI rabeprazole (10 mg/day) had been administered for 6 months before admission for prevention of peptic ulcer disease. His PD modality was automated peritoneal dialysis (2 exchanges of 1.5% 2.0-L glucose solution) and a 4-hour daytime dwell (1.5% of 2.0-L glucose solution). Mild dehydration, including dryness of the tongue, was observed on physical examination, and routine blood biochemistry showed a slight rise in the inflammatory marker C-reactive protein (0.36 mg/dL; normal < 0.03 mg/dL). On admission, he did not show any of the cloudy fluid or abdominal pain found in PD-associated peritonitis. *Clostridium difficile* toxin and other pathogenic bacteria were not detectable in stool cultures. Abdominal computed tomography showed diffuse edema of the colonic mucosa. Total colonoscopy was performed on hospital day 6, showing no signs of inflammation on the surface of the colon, and only a few diverticula and small polyps. Although gross appearance was unremarkable, mucosal biopsies of the colon were performed in several places (ascending colon, transverse colon, descending colon, cecum, and rectum). In these specimens, Congo-Red and direct fast scarlet staining yielded negative results, and gastrointestinal amyloidosis was excluded based on these histological findings. Masson's trichrome staining showed subepithelial collagen bands in every specimen (Fig. 1). Collagenous colitis associated with rabeprazole was thus suspected based on the histological finding, and the prescription was changed from rabeprazole to polaprezinc (150 mg/day). After changing drugs, the number of episodes of watery diarrhea each day was reduced within a few days. By 1 month after discontinuing rabeprazole, watery diarrhea had completely disappeared.

DISCUSSION

Numerous reports of collagenous colitis have been made already in the United States and Europe, where collagenous colitis is regarded as an important disease in the differential diagnosis of chronic watery diarrhea. In contrast, collagenous colitis remains not very well known in Japan. However, reports on collagenous colitis caused by PPIs in HD patients have increased in recent years (4–5). Diagnosis of collagenous colitis involves confirmation of a collagen band of <10 μ m thickness in biopsy tissue obtained by colonoscopy. However, some cases of collagenous colitis in which perforation occurred during radiographic contrast enema and after colonoscopy have also been reported (6). Hence, air insufflation of the colon should be minimized during the procedures. Collagenous colitis has been reported to be complicated by gastrointestinal perforation in less than 1% of cases (7). Dialysis patients with cardiovascular disease as a complication often take anti-platelet drugs such as clopidogrel and/or anticoagulants such as warfarin. In such patients, the prevalence of peptic ulcer is known to be high. A recommendation has therefore been made that PPIs should be prescribed at the same time as anti-platelet drugs for the purpose of preventing peptic ulcer (8). In particular, rabeprazole offers

Figure 1 — Staining with Masson's trichrome identified collagen bands (white arrow). These bands of collagen stained blue with the trichrome stain and negative for amyloid with Congo-Red stain and direct fast scarlet staining.

rapid effects against gastroesophageal reflux disease. Furthermore, rabeprazole is considered safer than omeprazole or lansoprazole, because the effects of rabeprazole against gastroesophageal reflux disease are not influenced by CYP2C19 polymorphism (9). Many cases of collagenous colitis in hemodialysis patients have been attributed to lansoprazole. However, our patient on PD developed collagenous colitis due to rabeprazole. Patients on PD often experience exacerbation of gastroesophageal reflux disease due to accumulation of intraperitoneal dialysate (10). We thus believe that PD patients may be at higher risk of collagenous colitis because they are taking PPIs at a relatively high frequency. Furthermore, we have concerns about the incidence of perforation due to collagenous colitis.

In conclusion, we reported a case of PD complicated by collagenous colitis. The cause of collagenous colitis was rabeprazole, and chronic watery diarrhea improved after discontinuation of the drug. Collagenous colitis is important as one of the differential diagnoses for chronic watery diarrhea, and should be suspected when a PD patient develops watery diarrhea while taking PPIs.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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