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【 CASE REPORT 】

Evaluation by MR Enterocolonography of Lansoprazole-induced Collagenous Colitis Accompanied with Protein-losing Enteropathy

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Abstract:

We herein describe a 69-year-old man suffering from chronic diarrhea caused by lansoprazole (LPZ)-induced collagenous colitis (CC) accompanied with protein-losing enteropathy (PLE), diagnosed by increased fecal alpha-1 antitrypsin clearance and the findings of leakage from the descending colon to the sigmoid colon on scintigraphy. MR enterocolonography (MREC) was also performed for differentiating digestive diseases, and inflamed findings were observed around the same portion as those on scintigraphy, suggesting that this region was responsible for protein loss in this case. The MREC findings improved after the cessation of LPZ, and hypoalbuminemia also improved simultaneously. This case suggests that MREC may be a new and useful diagnostic tool for CC with PLE.

Key words: collagenous colitis, MR enterocolonography, lansoprazole, protein-losing enteropathy

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Introduction

Collagenous colitis (CC), characterized by the deposition of a collagen band in the colonic sub-epithelium, is supposed to be the cause of persistent diarrhea (1), while also rarely leading to protein-losing enteropathy (PLE) (2-5). The pathophysiology of CC is still unclear, but some drugs such as proton-pump inhibitors (PPIs), especially lansoprazole (LPZ), and non-steroidal anti-inflammatory drugs (NSAIDs) are reported to be causative or triggering agents and the cessation of these drugs can sometimes improve the diarrhea symptoms (1).

Recently, MR enterocolonography (MREC) has been reported to be clinically useful to evaluate the intestinal lesions of Crohn's disease (CD) (6-8), especially in those that are impossible to observe endoscopically due to stenosis. In addition, we also reported the high sensitivity and specificity of MREC to detect mild lesions, such as wall thickness and edema of CD (8). Hence there is a possibility that MREC could be useful for identifying intestinal lesions in other diseases.

We experienced the rare case of a 69-year-old man suffering from persistent diarrhea due to CC with PLE induced by LPZ. The time course changes of colonic inflammation were analyzed by MREC before and after the cessation of LPZ and the change in findings with improving abdominal symptoms suggest that the MREC could be a new and useful diagnostic and monitoring tool for CC with PLE.

Case Report

A 69-year-old man had been suffering from persistent diarrhea for about 10 months even after being treated with antidiarrheal and salazosulfapyridine. He was referred to our hospital. He was admitted emergently when his diarrhea got

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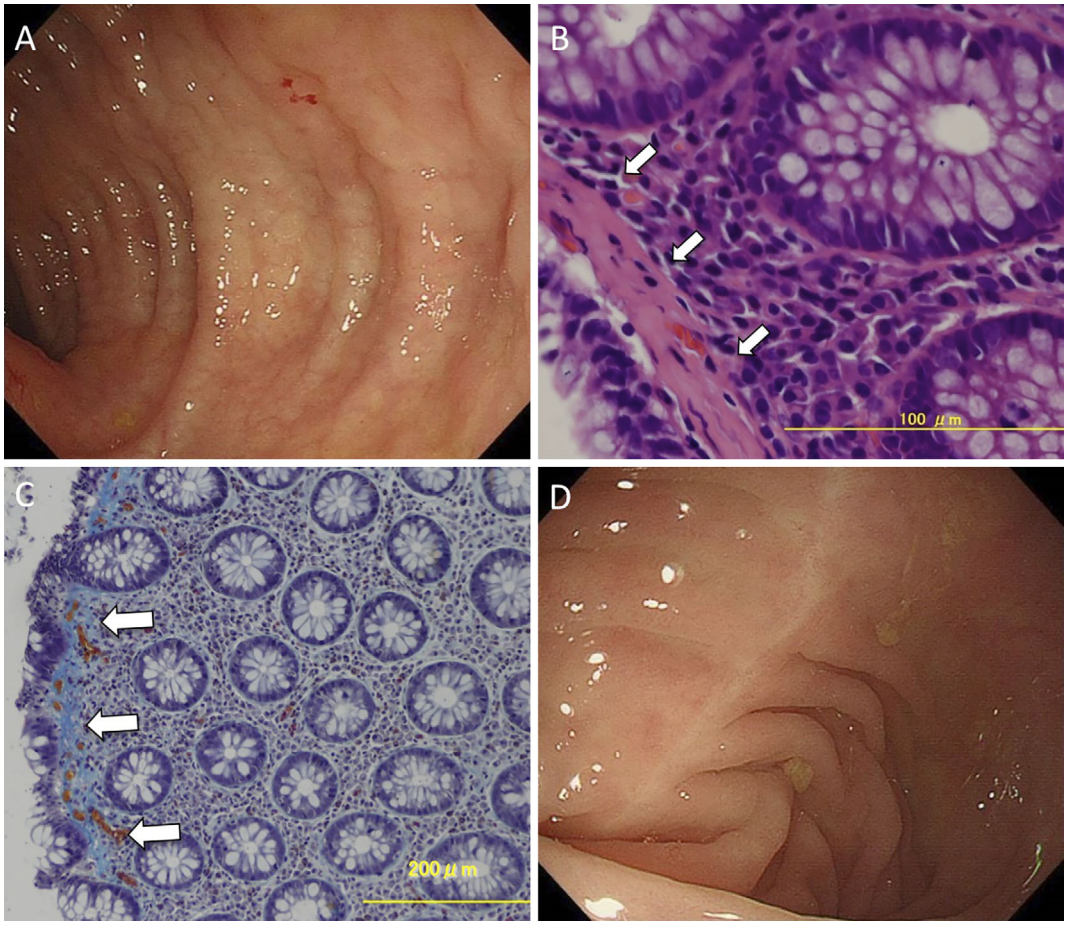

Figure 1. **Colonoscopical and histological findings of CC. A: Colonoscopy before the cessation of LPZ showed a slightly edematous mucosa in the sigmoid colon. B: Colonic mucosa stained by Hematoxylin and Eosin staining. The arrows indicate a collagen band in the colonic sub-epithelium. C: Colonic mucosa stained by Masson trichrome. The arrows indicate a collagen band. D: Colonoscopy 3 months after the cessation of LPZ showed a longitudinal ulcer scar characteristic of CC on the sigmoid colon.**

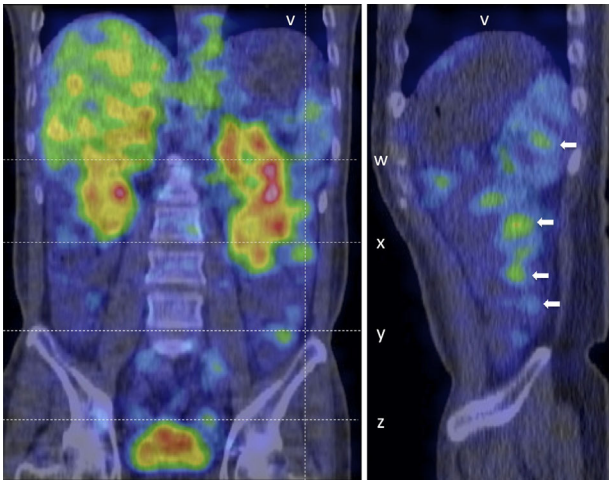

Figure 2. **Image assessment of CC with PLE on admission by coronal and sagittal views of ^{99m}Tc-HSA scintigraphy. The sagittal view is cut along the dashed line v of the coronal view. The arrows show the leakage from the descending colon. The dashed lines w, x, y and z are cut lines of axial images shown in Fig. 3. ^{99m}Tc-HSA: ^{99m}Tc-human serum albumin**

worse with severe dehydration and the laboratory data on admission showed hypoalbuminemia (1.9 g/dL, normal range is between 3.8 and 5.3 g/dL) and hyponatremia (128 mEq/L). He had diabetes mellitus and thus had been regularly treated with insulin, but the disease was in poor control (fast blood glucose was 481 mg/dL and HbA1c was 8.7%). He was examined colonoscopically and diagnosed to have CC histologically. Colonoscopy showed a slightly edematous mucosa in the sigmoid colon (Fig. 1A) and colonic specimens showed a collagen band according to hematoxylin and eosin (HE) staining (Fig. 1B) and Masson trichrome staining (Fig. 1C). His fecal alpha-1 antitrypsin clearance was 99mL/day (normal is below 27mL/day). Technetium-99 m-labeled human serum albumin (^{99m}Tc-HSA) scintigraphy showed slight leakage in the descending and sigmoid colon after 24 hours (Fig. 2, 3). MREC was also performed for differentiating other digestive diseases, which showed wall hyperintensity from the descending colon to the sigmoid colon on diffusion-weighted imaging (DWI, Fig. 3). No significant change was observed on the T2-weighted imaging (T2WI, Fig. 3). The findings in DWI were observed around the

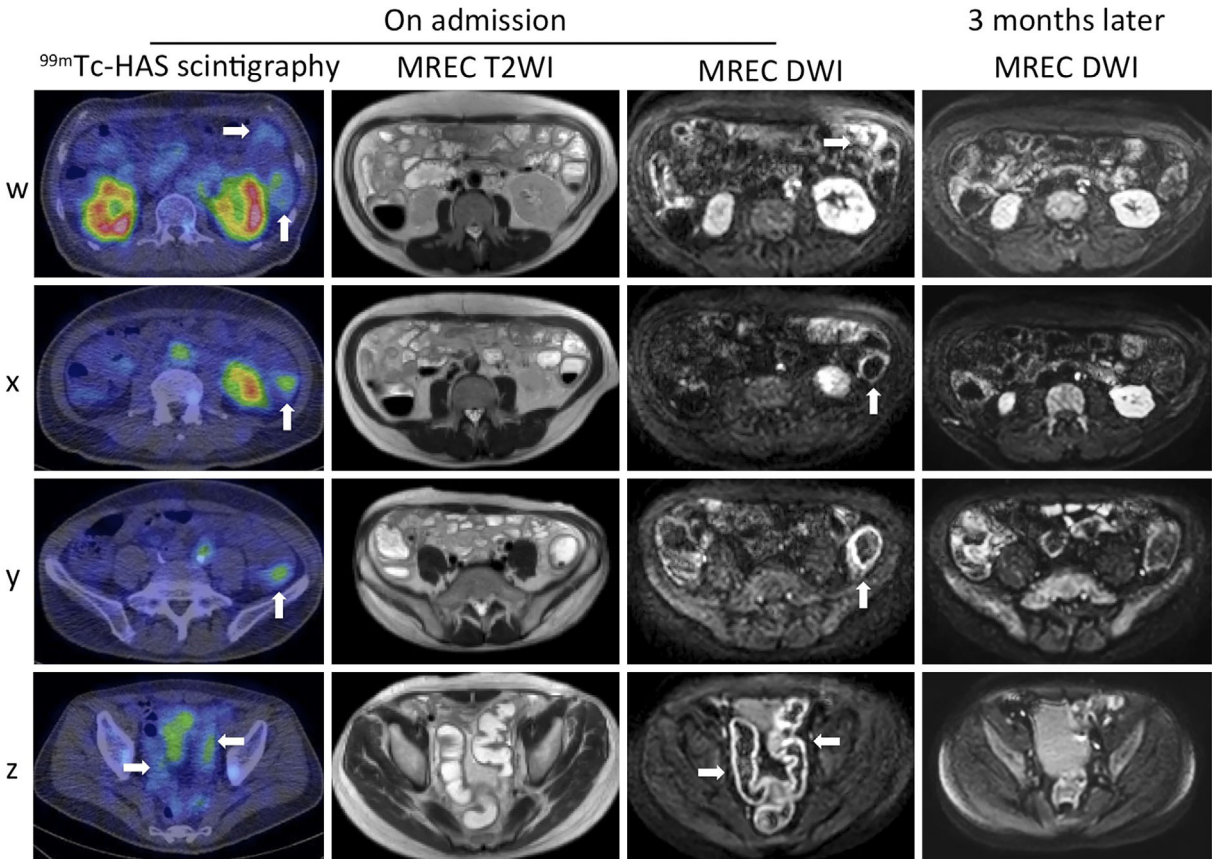

Figure 3. **Representative axial images of ^{99m}Tc-HSA scintigraphy, T2WI and DWI in the 1st MREC on admission, and DWI in the 2nd MREC 3 months after the cessation of LPZ. All the images are axial views cut along dashed lines w, x, y, and z in Fig. 2, respectively, in descending order. Scintigraphy is the same examination of Fig. 2, showing some leakage from the descending colon to the sigmoid colon indicated by arrows. No remarkable finding was observed in T2WI. In DWI on admission, the sigmoid and descending colons showed expansive strong intensity as indicated by arrows. DWI in MREC 3 months after the cessation of LPZ showed improved inflammatory findings. ^{99m}Tc-HSA: ^{99m}Tc-human serum albumin, DWI: diffuse-weighted imaging, T2WI: T2-weighted imaging**

same portion as those on scintigraphy, suggesting that the portion with hyperintensity was responsible for the loss of protein. Based on these findings, we diagnosed the patient to have CC accompanied with PLE.

Until then, he had continuously taken LPZ (30 mg/day) prescribed at another hospital to prevent the side effects of gastric bleeding by the combined usage of anti-platelet therapy (aspirin and clopidogrel) after percutaneous coronary intervention. We thought that LPZ was thus a causal agent, and after the cessation of LPZ his abdominal symptom gradually improved and his serum albumin level increased to 4.4 g/dL 3 months later. Second MREC was also performed and the inflammatory findings improved in the descending colon and sigmoid colon on DWI (Fig. 3). Colonoscopy was performed and a characteristic longitudinal ulcer scar was observed in the sigmoid colon (Fig. 1D), and lymphoid follicles were not so clear as before. Colonic specimens taken by a step biopsy from all the parts of the colon showed a collagen band even after the improvement in his clinical symptom and MREC findings.

Discussion

We herein present a rare case of CC with PLE, whose inflammatory condition was analyzed by MREC before and after achieving an improvement of the abdominal symptoms and hypoalbuminemia.

The usefulness of MREC for CD has been confirmed in several reports including our previous report (8), and DWI high intensity is a good predictor of endoscopic intestinal inflammation. In this case, we consider that MREC detected the area responsible for protein loss based on the following reasons: 1. The ^{99m}Tc-HSA positive area in the lower colon was the same as that observed with a DWI high intensity area on MREC, 2. Nearly simultaneous improvements were observed for hypoalubiminemia and the MREC findings after the cessation of LPZ, and 3. A longitudinal ulcer scar was observed in the sigmoid colon subsequently. Of course, it is impossible to diagnose CC based on the MREC alone without pathological examinations and we have not yet found any specific findings of CC on MREC. However,

since MREC is useful for evaluating the degree of inflammation in the gastrointestinal tract, MREC might be useful for detecting protein loss from the lesion and also for performing follow-up investigations of inflammation and the clinical course. On the contrary, bowel preparation is poorly tolerated in some cases in daily practice and there is a report that conventional DWI-MRI, MRI without bowel preparation, is a reliable tool for detecting colonic inflammation in inflammatory bowel disease (IBD) (9). Therefore, after we found the responsible lesion to be located only in the colon, then conventional MRI might be sufficient to follow up the inflamed lesion.

We should confirm the usefulness of this modality by comparing the findings from the patients of CC with PLE and the findings from the patients without PLE, but we have so far had no other patients with CC examined by MREC. However, in this case, we could compare the lesions of CC with protein loss and the lesions of CC without protein loss. In addition, ^{99m}Tc-HSA scintigraphy has been reported to be useful for detecting lesions associated with protein loss (10). In this case, ^{99m}Tc-HSA was positive only in the descending and sigmoid colon, while it was negative in the right hemicolon. However, a collagen band was observed in all regions of the colon. Thus, right hemicolon had CC lesions without PLE, and the colon from the descending colon to the sigmoid colon had CC lesions with PLE. The inflammatory findings of MREC were positive in the sigmoid and descending colon, which overlapped with the positive lesions observed on ^{99m}Tc-HSA scintigraphy.

In our present case, hypoalbuminemia improved soon after the cessation of LPZ in accordance with the improvement of MREC findings. We hypothesized that LPZ was related to hypoalubuminemia/PLE and investigated our previous CC cases. There were 7 CC cases including the present case (between 2005 and 2015) and we found that the value of 3 CC cases with LPZ is considerably lower (2.6±0.8 g/dL) than that of the other 4 CC cases without LPZ (4.4±0.1 g/dL). This result suggests that the intestine is severely damaged in LPZ-induced CC and thus suffers protein loss, although the quantification of fecal protein was not clarified except in present case. In addition to our investigation, there are already 4 case reports of CC with PLE (2-5), two from the USA and two from Japan. Among the 5 cases including ours, LPZ was taken in 3 cases, which were only from Japan (100% in Japanese cases of CC with PLE) (3, 5). This result also implies that LPZ might be a possible causal agent of hypoalbuminemia/PLE, especially in Asian patients.

It is reported that LPZ and NSAIDs are independent risk factors for CC (11). In our case, aspirin was also administered to the patient, but the causal agent was assumed to be LPZ because the symptoms improved soon after the cessation without any cessation of aspirin. Other studies in Japan reported a high rate consumption of LPZ in around 50-80% in CC cases, although in Europe, the consumption rate in CC cases is only 8.3% (11). Umeno et al. suggested that since LPZ is primarily metabolized in the liver by CYP2C19 and the prevalence of a poor metabolizer of CYP2C19 substrates is higher in Asians (15-30% vs. 3-6% in Caucasians), the differences in genetically determined drug-metabolising enzyme activities might contribute to the high occurrence of CC in Japan (12). The prevailing usage of new anti-acid drugs that act independently from CYP2C19, such as Potassium-Competitive Acid Blocker Vonoprazan, might therefore decrease CC in Japan in the future.

Conclusion

This report suggests that MREC DWI might be useful for evaluating CC with PLE. Since MREC is less invasive and more sensitive than endoscopic examinations in some cases, there should be more studies conducted to investigate the clinical usefulness of this modality.

The authors state that they have no Conflict of Interest (COI).

References

1. Ohlsson B. New insights and challenges in microscopic colitis. Therap Adv Gastroenterol **8**: 37-47, 2015.
2. Almadhoun OF, Katzman PJ, Rossi T. Collagenous colitis associated with protein losing enteropathy in a toddler. Case Rep Gastrointest Med **2014**: 209624, 2014.
3. Sano S, Yamagami K, Tanaka A, et al. A unique case of collagenous colitis presenting as protein-losing enteropathy successfully treated with prednisolone. World J Gastroenterol **14**: 6083-6086, 2008.
4. Stark ME, Batts KP, Alexander GL. Protein-losing enteropathy with collagenous colitis. Am J Gastroenterol **87**: 780-783, 1992.
5. Ozeki T, Ogasawara N, Izawa S, Mizuno M, Yanamoto K. Protein-losing enteropathy associated with collagenous colitis cured by withdrawal of a proton pump inhibitor. Intern Med **52**: 1183-1187, 2013.
6. Hordonneau C, Buisson A, Scanzi J, et al. Diffusion-weighted magnetic resonance imaging in ileocolonic Crohn's disease: validation of quantitative index of activity. Am J Gastroenterol **109**: 89-98, 2014.
7. Fujii T, Naganuma M, Kitazume Y, et al. Advancing magnetic resonance imaging in Crohn's disease. Digestion **89**: 24-30, 2014.
8. Sato H, Tamura C, Narimatsu K, et al. Magnetic resonance enterocolonography in detecting erosion and redness in intestinal mucosa of patients with Crohn's disease. J Gastroenterol Hepatol **30**: 667-673, 2015.
9. Oussalah A, Laurent V, Bruot O, et al. Diffusion-weighted magnetic resonance without bowel preparation for detecting colonic inflammation in inflammatory bowel disease. Gut **59**: 1056-1065, 2010.
10. Khalesi M, Nakhaei AA, Seyed AJ, et al. Diagnostic accuracy of nuclear medicine imaging in protein losing enteropathy : systematic review and meta-analysis of the literature. Acta Gastroenterol Belg **76**: 413-422, 2013.
11. Fernandez-Banares F, de Sousa MR, Salas A, et al. Epidemiological risk factors in microscopic colitis: a prospective case-control study. Inflamm Bowel Dis **19**: 411-417, 2013.
12. Umeno J, Esaki M, Nuki Y, Kim H, Kitazono T, Matsumoto T. Letter: lansoprazole consumption is more common in Japanese patients with collagenous colitis. Aliment Pharmacol Ther **38**: 208-209, 2013.

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