

# Acute onset collagenous colitis associated with protein-losing enteropathy

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## Abstract

Collagenous colitis is a cause of chronic diarrhea. We report an atypical case of collagenous colitis, presenting with an acute onset, and associated with protein-losing enteropathy. An 82-year-old woman was admitted with a 1 week history of nausea, appetite loss, and diarrhea. Serum albumin level was low. Protein leakage from the small intestine was found by a Technetium-99m human serum albumin scintigraphy. We diagnosed the patient with collagenous colitis from pathology findings of multiple biopsies taken from the colon. This case implies that collagenous colitis should be considered in acute watery diarrhea, and that it can cause protein-losing enteropathy.

## KEYWORDS

acute onset, aspirin, collagenous colitis, lansoprazole, protein-losing enteropathy

## 1 | INTRODUCTION

Collagenous colitis is an inflammatory bowel disease, characterized by chronic watery diarrhea. The onset is usually insidious, and the association of protein-losing enteropathy is rare. Pathogenesis is unclear, but smoking and medications including aspirin and lansoprazole have been reported to be important risk factors.<sup>1,2</sup> Diagnosis relies on colonic mucosal biopsy to rule out other bowel diseases. The typical histologic findings are subepithelial collagen bands more than 10  $\mu\text{m}$  in thickness and lamina propria inflammation.

We experienced an atypical case of collagenous colitis presenting as acute watery diarrhea, associated with protein-losing enteropathy.

## 2 | CASE PRESENTATION

An 82-year-old woman with a past history of chronic kidney disease and thyroid cancer (post-thyroidectomy) was admitted to our hospital due to a 1 week history of nausea, appetite loss, and diarrhea. Three days before the onset of symptoms, she visited a nearby clinic complaining of a chronic cough. The physician prescribed levofloxacin suspecting infection. A few days later, the diarrhea started, which brought her to stop taking the levofloxacin 3 days before admission. She had no history of smoking, recent traveling, and no particular family history.

On examination, vital signs were stable. There were no significant findings except bilateral pitting edema in the lower extremities, which

had manifested in the past week. The laboratory data indicated a low serum albumin level of 1.6 g/dL, which was 3.1 g/dL 2 months ago. Medications included aspirin, lansoprazole, and levothyroxine. The aspirin and lansoprazole had been prescribed for at least 2 years, but we could not find out why.

Our first differential diagnoses for this patient were antibiotic-associated diarrhea or *Clostridium difficile* infection. For antibiotic-associated diarrhea, we suspected levofloxacin to be the cause. The patient had already stopped taking it. For *C. difficile* infection, the possibility was less likely as *C. difficile* antigen/toxin test results were both negative. We decided not to add any medication, and the symptoms spontaneously improved in a few days. She was discharged on the fifth postadmission day.

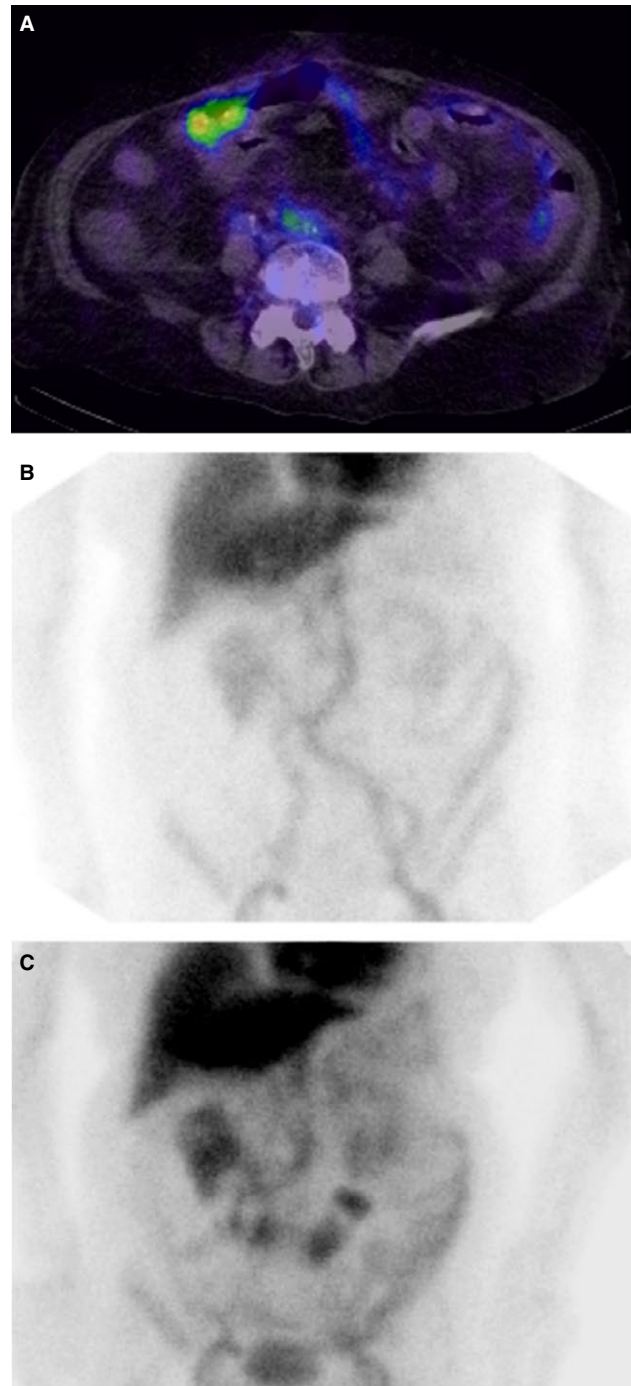
However, 4 days later, the patient was readmitted to our hospital due to the recurrence of diarrhea. The serum albumin level decreased to 1.2 g/dL. Stool occult blood was positive, but gram stain, culture, and fat stain of the stool showed no particular findings. There was no proteinuria, liver dysfunction, or any sign of hypermetabolism that could lead to the low serum albumin. An enhanced CT scan of the abdomen showed bowel wall thickening and fat stranding. There were no signs of vascular obstruction, pancreatitis, or endocrine tumors. Suspecting protein leakage from the small intestine and colon, we performed a Technetium-99m human serum albumin scintigraphy. It showed protein leakage from the small intestine (Figure 1A-C) proving the existence of protein-losing enteropathy. Fasting and total parenteral nutrition were initiated, which did not improve the diarrhea, indicating that it did not result from malabsorption. To identify any structural disorders, an endoscopy of the stomach, duodenum, and colon was performed. No obvious abnormalities were revealed from the stomach and duodenum. Diffuse edema was observed throughout the colon (Figure 2A) as well as a few polyps. Biopsy was taken from multiple regions. There were no signs of malignancy, amyloidosis, or eosinophilic gastroenteritis. Mild inflammation was found in samples taken from the duodenum. Samples of the ascending colon showed subepithelial collagen bands more than 10  $\mu\text{m}$  in thickness as well as lamina propria inflammation (Figure 2B,C). With these findings, we reached the diagnosis of collagenous colitis.

We discontinued aspirin and lansoprazole, and after the introduction of loperamide, the diarrhea and serum albumin level improved.

### 3 | DISCUSSION

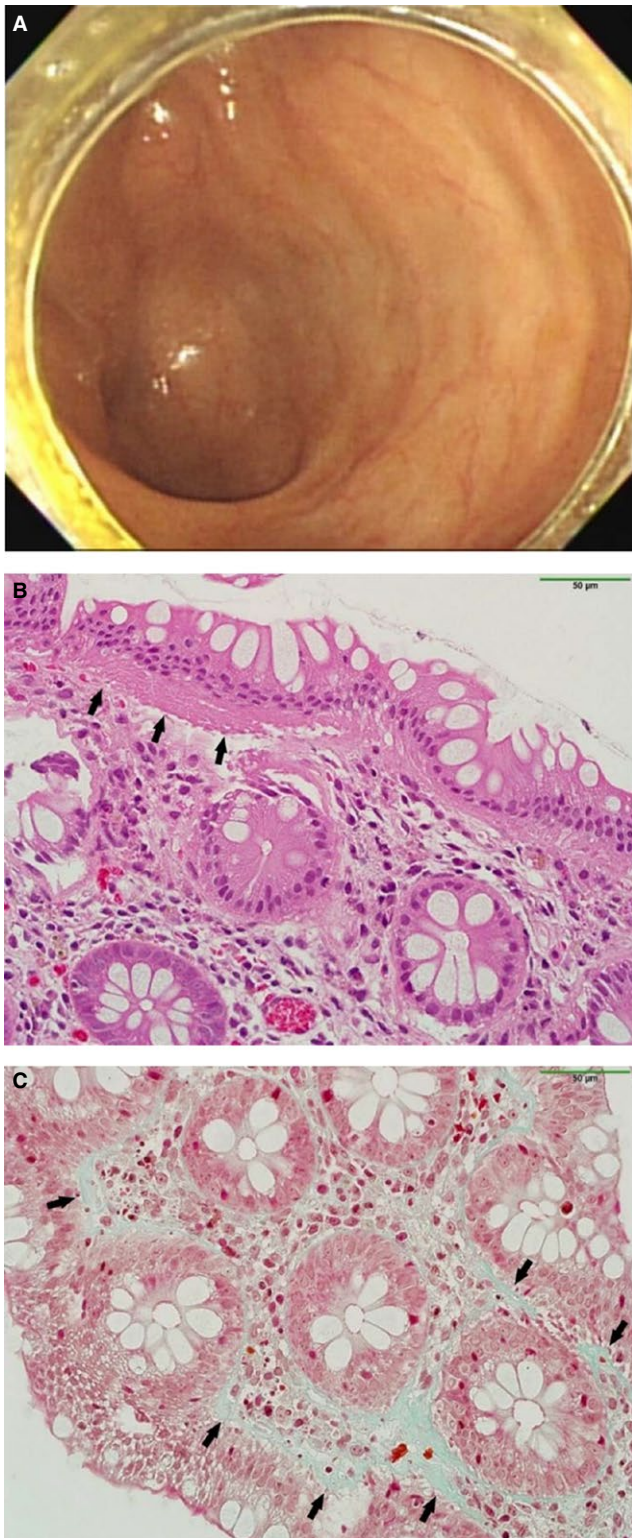
We discovered two important clinical issues from this case. First, collagenous colitis can present as acute onset diarrhea instead of chronic. Second, it can also cause protein-losing enteropathy.

The onset of collagenous colitis is usually insidious, and the clinical course is mostly chronic relapsing and benign.<sup>1,2</sup> However, in a retrospective study of 163 cases, 42% presented with an acute onset.<sup>3</sup> There are also reports of collagenous colitis with a presentation similar to ischemic colitis, which is different from this case.<sup>4,5</sup>



**FIGURE 1** (A) Technetium-99m human serum albumin scintigraphy showing protein leakage from the small intestine. (B) Anterior image 2 h after injection. (C) Anterior image 6 h after injection. Showing abnormal exudation of radiotracer to the bowel

The accurate epidemiology of acute diarrhea is very difficult to determine. This is because not all patients present to health services, and as many cases improve spontaneously, many presenting cases are not investigated further. In one study carried out in Tokyo, Japan, fecal samples from 1564 patients diagnosed as infantile diarrhea or infectious gastroenteritis were studied. The cause was unknown in 53.8% of the cases.<sup>6</sup> Considering the high proportion of unknown causes,



**FIGURE 2** (A) Colonoscopy showing diffuse edema throughout the colon. (B) Hematoxylin and eosin stain. (C) Masson trichrome stain

there is a possibility that a certain number of cases of collagenous colitis are hidden in this population.

Association of protein-losing enteropathy is generally acknowledged to be rare, and we could not find any studies on the actual frequency. In some case reports, protein leakage from the colon

was identified by Technetium-99m human serum albumin scintigraphy.<sup>7,8</sup> With the same method, we were able to prove the existence of protein-losing enteropathy in this case.

Collagenous colitis has been linked to several medications such as nonsteroidal anti-inflammatory drugs and proton pump inhibitors,<sup>1,9</sup> but convincing evidence is lacking. The patient in this case was taking aspirin and lansoprazole, and we decided to stop them as she had no obvious underlying cardiovascular or cerebrovascular disease. In our daily medical practice, we see patients with multiple medications. This so-called “polypharmacy” is associated with an increased risk of adverse events.<sup>10</sup> We should always be aware of what medications our patients are taking and why. By doing so, it may lead to reducing the frequency of adverse events and even the prevalence of collagenous colitis.

The unusual presentation of this case made the diagnostic process difficult. In cases of acute onset diarrhea associated with hypoalbuminemia, collagenous colitis should be taken into consideration, and medications must be checked.

#### 4 | CONCLUSION

We reported an atypical case of collagenous colitis with an acute onset, associated with protein-losing enteropathy. Collagenous colitis is known to be a cause of chronic watery diarrhea, but it should also be considered in cases of acute onset diarrhea. It can also cause protein-losing enteropathy.

#### CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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