Collagenous Colitis

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We report a case of 76-year-old male with a complaint of watery diarrhea due to collagenous colitis. Biopsy specimens from the sigmoid colon showed a thick subepithelial collagen band, which were immunoreactive for collagen types 1, 3, 5 and 6. We started salazopyrine as the treatment of collagenous colitis but observed no effect, then changed to prednisolone 30mg per day. After the treatment with prednisolone, his symptoms had completely improved. The results of this case suggest that prednisolone may be useful and can lead to the complete remission in the treatment of collagenous colitis. (Kitakanto Med J 2002 ; 52 : 283–285)

Key words : collagenous colitis, prednisolone, collagen typing, treatment

Introduction

Collagenous colitis was first reported in 1976 by Clas Lindström.¹ The patient was a 48-year-old female with chronic watery diarrhea who showed a remarkable subepithelial collagenous deposit histologically. Since then, numbers of similar cases have been reported, the present report describes a case of collagenous colitis whose symptoms were completely resolved by prednisolone.

Case Report

A 76-year-old male visited our hospital because of watery diarrhea for 3 days on August 9, 1999. After anti-diarrheal drugs had proved ineffective, he was admitted for further examination on August 23, 1999. A physical examination on admission showed slight abdominal distension. The results of blood examination were within normal ranges. Plain abdominal roentgenograms showed slight gaseous distension of the large bowel. A barium enema disclosed decreased haustral markings in the sigmoid colon. Colonoscopy showed only slight mucosal roughness in the sigmoid colon.

Microscopic analysis of the sigmoid colon biopsy showed a band of collagen fibers beneath the surface epithelium and mildly inflammation in the lamina propria. Indirect immunoperoxidase study revealed deposition of collagenous material in the band of deposits, which were immunoreactive for collagen types 1, 3, 5 and 6. Type 4 collagen was located along the basement membrane and type 2 collagen was negative. Amyloid P component, CD34, and alpha-smooth muscle actin were also negative. The thickness of the collagen band beneath the surface epithelium ranged 7.50 to 43.10μm in width (Fig. 1,2). Thus, we diagnosed the case as collagenous colitis.

We started administration of sulfasalazine (salazopyrine) on September 4, 1999 but which was ineffective. Prednisolone 30mg per day completely resolved symptoms.

Fig.1 Histologic appearance of colonic biopsy specimen. Band of eosinophilic collagen fibers are located just beneath the overlying epithelial layer. (×100)
cleared the patient's symptoms. After initiating treatment with prednisolone, biopsy specimens were taken from the transverse colon, descending colon, sigmoid colon and rectum. The descending colon and sigmoid colon were still affected, while the other regions showed no abnormalities. We decreased the dosage by half every five days, and at last complete remission was achieved in July 2000.

Discussion

Collagenous colitis is characterized by chronic watery diarrhea, diffuse inflammation of the colonic mucosa, and a thick band of subepithelial collagen fibers. Since the first report by Clas Lindstrøm, more than 500 cases of collagenous colitis have been described. The incidence of collagenous colitis is between 0.6 and 2.3/100,000 inhabitants. Patients are usually middle-aged women. Allegedly, the disease is very rare among the Japanese. The onset of collagenous colitis is mostly insidious, but 42% of patients show a sudden onset. The clinical course is chronic and intermittent, and single episodes are rare. All patients accompany watery diarrhea as a primary symptom and nocturnal diarrhea is also common. Bloody or mucinous stool is uncommon and stool culture showed no infectious features. The stool frequency is variable but up to 30 bowel movement per day. Other symptoms of collagenous colitis include abdominal pain and mild weight loss.

The pathogenesis of collagenous colitis is still unknown. The variety of autoimmune diseases has been reported to be associated with this colonic abnormality, and the most common concomitant disorders include rheumatoid arthritis, thyroid disorders and celiac disease. This suggests that an autoimmune mechanism should be considered in collagenous colitis, although our case had no autoimmune disorders. In a recent report, Ung et al. suggested that bile acids and bile acid binding agents played an important role in patients with collagenous colitis. The bile salts and bacterial toxins are considered to be one of the factors causing collagenous colitis, forty-four percent of the patients with collagenous colitis showed bile acid malabsorption by 75Se-homocholic acid taurine test. These patients were prescribed bile acid binders (cholestyramine or colestipol) and showed good responses.

The affected lesions appear in widespread distribution in the colon, while they are often patchy and localized mainly in the proximal colon. For this reason, biopsy specimens must be taken from proximal to the sigmoid colon.

The characteristic pathological findings is a sube-
pithelial band of collagen fibers more than 10 µm in width, in association with chronic inflammation.\textsuperscript{4} Immunohistochemically, the presence of collagen types 1, 3, 4, 6, and the expression of noncollagenous matrix components such as tenascin has been reported.\textsuperscript{5,13,14} Collagen types 1 and 3 are usually involved in tissue repair processes, and the thickening of the subepithelial collagen band may be a result of inflammation.\textsuperscript{4} Our case showed only a mild inflammatory cell infiltration and no apparent tissue damage or major inflammation was noted. Collagen type 5 is reportedly increased in the mucosa of Crohn’s disease and it leads to a loss of the normal compliance of the intestine and to thickening of the intestine wall.\textsuperscript{15}

No effective standard treatment for collagenous colitis has yet been established. Wang et al.\textsuperscript{16} reported an anti-inflammatory treatment (sulfasalazine, hydrocortisone, and prednisolone, alone or in combination) with an effectiveness rate of 66.7\% in patients with collagenous colitis. Prednisolone was effective in our case, whereas non-specific anti-diarrheal agents and sulfasalazine showed no effect.

Prednisolone has occasionally been used for collagenous colitis patients who are refractory to other therapy. Pimentel et al.\textsuperscript{6} reported that prednisolone produced the best response in such cases, resulting in complete resolution of symptoms in 9 of 10 patients who had poor response to previous therapy. However, Bohr\textsuperscript{2} reported the effect of prednisolone was not sustained, with frequent relapses after withdrawal of the treatment. Lanyi et al.\textsuperscript{8} reported the usefulness of budesonide for the patient with prednisone-refractory collagenous colitis. They used budesonide 9 mg/day for 3 to 7 months for three female patients and the symptoms were improved in all cases. Budesonide is a topically acting steroid and has a tissue affinity higher than prednisone, which might lead to a good response.\textsuperscript{8}

Our case received prednisolone for 32 days and obtained a complete remission without continuous prednisolone. He has not experienced complete histologic resolution despite the disappearance of his symptoms. Histologic changes usually correlate with clinical features; however, cases of clinical remission without histologic changes have also been reported.\textsuperscript{10,12} The reason for the discrepancy in our case is not clear, but may be related to the short time period until the follow-up colonoscopy after the administration of prednisolone.

In conclusion, the results of this case suggest that prednisolone may be useful and can lead to the complete remission in the treatment of collagenous colitis when non-specific anti-diarrheal agents or sulfasalazine are ineffective.

\textbf{References}