Human Intestinal Spirochaetosis in Two Ulcerative Colitis Patients

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Abstract

A histological examination of colonic biopsies of the longitudinal and irregularly-shaped ulcerative lesions of a 37-year-old man and 61-year-old man with ulcerative colitis showed so-called “fringe formation,” a typical finding of Brachyspira infection. The antibody titer to Brachyspira aalborgi showed marked elevation in both cases, and the patients were each treated with 1,000 mg of metronidazole for 14 days. Colonoscopy performed after treatment showed an improvement in the ulcerative lesions in both patients. These results indicate the possibility that intestinal spirochaetosis infection should be considered as an infectious complication in patients with ulcerative colitis receiving long-term steroid therapy.

Key words: human intestinal spirochaetosis, Brachyspira aalborgi and Brachyspira pilosicoli, ulcerative colitis, metronidazole


Introduction

Human intestinal spirochaetosis (HIS) was first reported by Harland and Lee in 1967 (1). HIS is a disease of the colorectum caused by the Gram-negative bacteria Brachyspira aalborgi and Brachyspira pilosicoli (2). B. pilosicoli causes disease in humans and in various animals, whereas B. aalborgi induces colonic spirochaetosis in humans only (3, 4).

The definitive diagnosis of HIS requires the use of polymerase chain reaction, electron microscopy (5), imprint cytology (6) and detection of serum antibody titers to Brachyspira aalborgi and Brachyspira pilosicoli with agglutination titers (7).

Human colonic spirochaetosis is common in developing countries, although it is relatively rare in industrialized countries, with high rates in homosexuals and HIV-infected individuals (2, 3, 8). A previous study demonstrated that HIS is associated with various intestinal diseases, including colon carcinoma and colonic polyps (9, 10). Previous reports (9, 10) have also shown that HIS can be found in cases of ulcerative colitis. However, the detailed clinical features of HIS infection in ulcerative colitis patients are unclear.

We herein report two cases of HIS infection in patients with ulcerative colitis who showed clinical improvements following metronidazole treatment.

Case Reports

Case 1

Case 1 involved a 37-year-old man with a 12-year history of pan-ulcerative (total) colitis. He experienced diarrhea two or three times per day, sometimes with bloody stools. On admission, his body temperature was 36.6°C, and his pulse rate was 70 beats/min. Laboratory studies showed a hemoglobin concentration of 14.7 g/dL and an erythrocyte sedimentation rate of 13 mm/h. Colonoscopy showed mild erosive mucosa in both the sigmoid colon and rectum as well as a longitudinal ulcerative lesion in the transverse colon (Fig. 1). The patient was treated with mesalazine at a dose of 2,250 mg/day and prednisolone at a dose of 5 to 10 mg/day. His disease was responsive to therapy with prednisolone.
lone; however it was difficult to taper the dose of prednisolone. A stool examination for conventional enteric pathogens was negative, and both cytomegalovirus antigenemia and clostridium difficile tests were negative. Although antibody testing for amebic infection was not conducted, no endoscopic or histopathologic findings of such infections were observed. A histological examination of the colonic biopsy samples of the edematous and erosive mucosa showed so-called fringe formation (Fig. 2). The agglutination titers were compared between the human serum and strains of Brachyspira aalborgi and Brachyspira pilosicoli. The antibody titer to Brachyspira aalborgi was 616±33: 6,400, and the titer to Brachyspira pilosicoli was 189±12: 400 (Table 1). A diagnosis of HIS was therefore made, and the patient was treated with 1,000 mg of metronidazole for 14 days. Colonoscopy performed after the completion of treatment with metronidazole showed an improvement in the edematous mucosa of the ulcerative lesion in the transverse colon (Fig. 3), and a histological examination of colonic biopsy samples did not show any fringe formation. Furthermore, the patient’s diarrhea appeared to be reduced at follow-up several weeks after treatment.

Case 2

Case 2 involved a 61-year-old man with a 20-year history of distal ulcerative colitis. He experienced diarrhea four or five times a day, sometimes with bloody stools. His body temperature was 36.2°C, and his pulse rate was 63 beats/
min. Laboratory studies showed a hemoglobin concentration of 13.7 g/dL and an erythrocyte sedimentation rate of 15 mm/h. Colonoscopy showed an irregularly-shaped ulcerative lesion in the rectum (Fig. 4). The patient had an allergy to mesalazine, including the suppository form. He had been treated with prednisolone at a dose of 2.5 mg/day with a prednisolone (PSL) suppository. His disease was responsive to therapy with prednisolone; however, the ulcerative rectal lesion did not improve. A stool examination for conventional enteric pathogens was negative, as was a cytomegalovirus antigenemia test. Although antibody testing for amebic infection was not conducted, no endoscopic or histopathologic findings of such infections were observed. A histological examination of the rectal biopsy samples obtained from the ulcerative mucosa showed so-called fringe formation (Fig. 5). The antibody titer to *Brachyspira aalborgi* was 616±33: 6,400, and the titer to *Brachyspira pilosicoli* was 189±12: 800 (Table 2). A diagnosis of HIS was therefore made, and the patient was treated with 1,000 mg of metronidazole for 14 days. Colonoscopy performed after the completion of treatment with metronidazole showed an improvement of the ulcerative lesion in the rectum (Fig. 6), and a histological examination of colonic biopsy samples no longer demonstrated fringe formation. The patient’s clinical symptoms and rectal ulceration appeared to improve for several weeks after treatment.

**Discussion**

The clinical effects of HIS infection have been studied, with various findings showing that HIS infection causes problems such as chronic diarrhea and/or abdominal pain (5, 11, 12). A previous analysis of 209 HIS patients evaluated their symptoms as well as the effects of antibiotic treatment (5) and found that 51% of the patients suffered from diarrhea, while 46% suffered from abdominal pain. Furthermore, 84 of the 209 HIS patients were treated with antibiotics, such as metronidazole, 44 (52.4%) of whom showed improvements in their symptoms, indicating that the bacteria were eradicated with metronidazole (5). Another report demonstrated that 17 HIS-infected patients all suffered from either abdominal pain or gastrointestinal symptoms,
Figure 5. Histology of the colonic biopsy specimens showed fringe formation on the luminal side of the colonic surface epithelium (Hematoxylin and Eosin staining) (A, B).

Figure 6. Colonoscopy performed after treatment with metronidazole showed an improvement in the ulcerative lesion in the rectum (A, B).

particularly long-standing diarrhea (11). In the present two cases, the patients’ clinical symptoms, including diarrhea, improved after treatment of HIS, indicating the possibility that the clinical symptoms were caused by the HIS infection as well as the ulcerative colitis.

Furthermore, in several HIS case reports, edematous mucosa with multiple erythematous spots was detected in the ascending and proximal transverse colon, but not in the distal colon or rectum (13, 14). The colonoscopic findings in HIS patients show either non-specific ulceration of the ileocecal valve or extensive areas of ischemic ulcers (15). In the present cases, HIS was found in irregularly-shaped ulcers or extensive longitudinal ulcers. To the best of our knowledge, there are no previous reports regarding the endoscopic findings of HIS infection complicated with ulcerative colitis. Our results indicate that the presence of longitudinal or irregularly-shaped ulcers in patients with ulcerative colitis may suggest the complication of HIS infection.

Previous studies have investigated the frequency of HIS in the colon and its possible correlation with various diseases. For example, Delladestima K. et al. demonstrated that 12 of 24 HIS cases were associated with carcinoma of the large intestine, three cases with adenomatous polyps, one case of hemorrhoids with metaplastic polyps and two cases with ulcerative colitis (9). Furthermore, Jensen et al. documented HIS in cases of carcinoma or polyps of the colon and ulcerative colitis (10).

Recent reports have indicated that bacteria play an important role in the pathogenesis of mucosal inflammation in patients with ulcerative colitis (16, 17). In addition, previous studies have shown that *Fusobacterium varium* bacteria are present in a significant number of patients with active ulcerative colitis, indicating that *Fusobacterium varium* is an elusive pathogenic factor involved in the pathogenesis of ulcerative colitis (16). Another report suggested that the mucosa-associated microflora, especially that involving the *Bacteroides* species, plays an important role in the etiology of ulcerative colitis (17). Furthermore, several previous studies have suggested that resident enteric bacteria are necessary for the development of spontaneous colitis in animal experiments (18, 19).

To the best of our knowledge, the clinical features and course of cases of ulcerative colitis involving HIS have not been well characterized. In our two HIS-positive cases, the patients’ endoscopic findings and clinical symptoms did not improve with mesalazine, and both patients were treated
with long-term steroid therapy. Since the patients were classified as having a HIS infection based on histology and their antibody titers to *Brachyspira aalborgi* and *Brachyspira pilosicoli*, they received metronidazole and subsequently exhibited clinical and endoscopic improvements. Previous reports have demonstrated that treatment with metronidazole is effective for treating HIS infection (5, 20). Therefore, our results suggest that HIS infection may have an effect on steroid-dependent cases of ulcerative colitis.

It has also been suggested that colonic spirochaetosis is transmitted via the fecal-oral route from animals, such as pigs, dogs and birds (3). In addition, homosexual and HIV-infected individuals as well as those in developing countries are at high risk for this infection (2). However, neither of our patients had these risk factors, and the route of infection in each case remains unclear.

In conclusion, two ulcerative colitis patients receiving long-term steroid therapy were found to have HIS infection and exhibited a good clinical response after treatment with metronidazole. These results suggest that HIS infection should be considered as an infectious complication in patients receiving long-term steroid therapy. Further accumulation of similar cases is needed, as we cannot deny the possibility that Spirochaeta was a bystander in these cases.

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

**References**