Helicobacter heilmannii Associated Erosive Gastritis

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The spiral bacteria, *Helicobacter heilmannii* (*H. heilmannii*), distinct from *Helicobacter pylori* (*H. pylori*), was found in the gastric mucosa of a 71-year-old man without clinical symptoms. The endoscopic examination revealed erosive gastritis. Rapid urease test from the antral specimen was positive, but both culture and immunohistological staining for *H. pylori* were negative. Touch smear cytology showed tightly spiral bacteria, which were consistent with *H. heilmannii*. At the second endoscopy after medication regimen for eradication of *H. pylori*, inflammation was decreased and the rapid urease test was negative. The second cytology showed no evidence of *H. heilmannii*. Anti-*H. pylori* therapy may be a useful medication for *H. heilmannii*. (Internal Medicine 38: 240–243, 1999)

Key words: gastric spiral bacteria, touch smear cytology, eradication

Introduction

Since 1983 when Warren and Marshall (1) first described *Helicobacter pylori* (*H. pylori*) and its association with chronic gastritis, there have been many reports of microbiological and clinical studies about *H. pylori* infection. It has been generally accepted that *H. pylori* infection causes atrophic gastritis, gastric ulcer and duodenal ulcer. Recently, *H. pylori* has been suggested to be a promoter of gastric carcinoma and primary mucosa-associated lymphoid tissue (MALT) type gastric lymphoma.

Helicobacter heilmannii (*H. heilmannii*), another spiral bacterium in the human gastric mucosa, was reported by Dent et al in 1987 (2). Although its incidence is much less than that of *H. pylori*, *H. heilmannii* has been described in association with gastroduodenal diseases as well as *H. pylori*. We present a rare case of *H. heilmannii*-associated gastritis and review case of this bacterium in the clinico-histopathological literature.

For editorial comment, see also p 217.

Case Report

A 71-year-old man visited our clinic for annual check up endoscopic examination of the upper gastrointestinal tract in February 1997. He had no abdominal discomfort and had

previously been healthy. He had a clinical history of Hansen's disease (leprosy). His family history was noncontributory. He reported no history of smoking or alcohol, but earlier had a pet cat. Neither anemia nor jaundice was present. Abdomen was flat and soft. Liver, spleen and mass were not palpable. Laboratory data of our clinic was within the normal range. Serum anti-*H. pylori* immunoglobulin G (IgG) antibody (HELICO-G) was negative. Serum pepsinogen I was 63.0 ng/ml, pepsinogen II was 7.9 ng/ml, and the ratio of I/II (PG I/II) was 8.0. Serum gastrin was 52 pg/ml.

The existence of *H. pylori* was determined by the standard guideline proposed by the Japanese Society of Gastroenterology. Bacteriologic culture, rapid urease test and histologic examination were done for the biopsy specimens from both the fundic and the antral mucosa. The histological diagnosis of biopsy tissue was done by the specimens of HE staining, Giemza staining and immunohistochemical staining by polyclonal antibody against *H. pylori* (DAKO). The touch smear cytology specimens were stained by May-Grünwald-Giemsa staining. The first upper gastrointestinal endoscopy showed multiple eruptions and erosions in the antrum (Fig. 1). The biopsy specimen from the antral mucosa presented chronic gastritis with lymphocytic aggregation (Fig. 2).

Rapid urease test of the specimen from the antral mucosa was positive, but biological culture and microscopic histologic examination were negative for *H. pylori*. However, touch smear cytology from the antral mucosa showed peculiar spiral bacte-

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Figure 1. The first endoscopic examination showing erosive gastritis in the antrum.

Figure 2. Microscopic findings of the specimen from the antral mucosa showing chronic gastritis with lymphocytic aggregation (HE stain, $\times 100$).

ria, which were larger and more tightly coiled than *H. pylori* (Fig. 3). The described bacteria were not seen by the microscopic histologic examination of HE staining and Giemsa staining. We recognized these spiral bacteria as *H. heilmannii* based on their characteristic morphological feature.

With the patient's consent, triple combination therapy with omeprazole (20 mg/day), amoxicillin (1,500 mg/day) and ecabet sodium (4 g/day) was given for two weeks. A second endoscopic examination was done 4 weeks after the medication. In macroscopic findings, multiple erosions were improved and eruptions were only presented in the antrum (Fig. 4). Histologi-

Figure 3. Touch smear cytology of the antral specimen showing abundant corkscrew-shaped *Helicobacter Heilmannii* organisms (Giemsa stain, $\times 1,000$).

Figure 4. Second endoscopic examination after eradication revealed improvement of antral erosions.

cal findings of antral biopsy showed essentially normal gastric mucosa without lymphocytic aggregation (Fig. 5). The rapid urease test was negative in the specimen from the antral mucosa and touch smear cytology showed no spiral bacteria.

Discussion

In addition to *H. pylori*, there is another spiral organism in human gastric mucosa associated with gastroduodenal disease, which has been called *H. heilmannii*, also known as *Gastrospirillum hominis*. These two spiral organisms belong to

Figure 5. Microscopic findings of the specimen from the antral mucosa after eradication showing essentially normal gastric mucosa without lymphocytic aggregation (HE stain, $\times 100$).

the same genus in the microbiological classification.

The morphological feature of *H. heilmannii* is a tightly spiral, corkscrew-shaped body. There are 4 to 9 turns over the length with truncated ends flattened at the tips; it is 3.5–4.5 μm long and 0.8–0.9 μm in diameter, which is larger and more coiled than *H. pylori* (2–3). *H. heilmannii* is seen in the neck of the gland, in the mucosal surface within or beneath the mucus of the stomach (3).

Although the incidence of *H. heilmannii* infection is much less than that of *H. pylori*, its infection has been reported to be frequent related to gastric cancer (4), gastric ulcer (5), acute gastric mucosal lesion (6, 7), duodenal ulcer (8), duodenal erosion (9), functional dyspepsia (10), esophagitis (3), and chronic active gastritis (3, 11–14). Some authors reported *H. heilmannii* infection in pediatric cases (13, 15, 16).

Spiral organisms have been reported in the gastric mucosa in many animals since the 1880's. Weber and Schmittiel (17) described a spiral bacterium morphologically very similar to *H. heilmannii* in cats and dogs. Another report described the evidence of transmission of *H. heilmannii* to human gastric mucosa from pet dogs (18) and cats (5). An epidemiologic investigation reported that 70.3% of the patients infected with *H. heilmannii* had contact with domestic animals and pets (19). From these studies, pet animals or domestic animals may be responsible for the transmission of *H. heilmannii* to human gastric tissue. The present case had contact with a cat for a long time and *H. heilmannii* might have been transmitted from the cat.

To date, culture of *H. heilmannii* has not yet been established, and the diagnosis of this bacterium infection is based on its morphological identification by histological examination and tissue smear cytology. Debongnie et al (20, 21) described that tissue smear cytology is a useful method rather than histological examination. Some reports (11, 14) described that *H. heilmannii* was detected only by tissue smear cytology. Also in this case, the organisms were detected by touch smear cytology, but were not detected by histological examination.

Based on these reports and the present case, tissue smear cytology is thought to be an essential method for diagnosis of *H. heilmannii* infection. Rapid urease test for *H. heilmannii* infection was reported to be positive in some cases (9, 13, 22). In the present case, rapid urease test from the antral biopsy specimen was positive and changed to become negative after eradication. These results suggest that this organism has urease activity to some degree and rapid urease test and urea breath test are thought to be useful methods in the diagnosis of *H. heilmannii* infection.

A few reports about eradication of *H. heilmannii* infection have been published, but effective eradication therapy has not yet been determined. Successful medications for its eradication have been reported as follows: bismuth subcitrate (5, 18), combined minocycline and cimetidine therapy (12), combined sucralfate and omeprazole therapy (6) and a triple regimen of bismuth subcitrate, tetracycline and metronidazole. In contrast, a case of eradication failure with antimicrobial therapy was reported (3). Establishment of the regimen of eradication therapy for this bacterium is needed as well as for *H. pylori* infection.

In the present case, a 2-week therapy of omeprazole, amoxicillin, and ecabet sodium was successful for the eradication of this organism. Omeprazole and amoxicillin have antibiotic activity for *H. pylori*. Omeprazole and ecabet sodium have antiurease activity. This short course of combination therapy with proton pump inhibitors and antibiotics has won international recognition as a successful and suitable therapy regimen for the eradication of *H. pylori*. To our knowledge, only 3 cases have reported the use of anti-*H. pylori* eradication regimen in the treatment of *H. heilmannii* infection (23, 24). Because of the same genus, anti-*H. pylori* therapy is considered to be useful eradication for *H. heilmannii* infection.

The degree of inflammation of gastritis induced by *H. heilmannii* has been reported to be mild to severe in pathological findings. McNulty et al described that a variety of types of inflammation of gastritis might be depended on the number of *H. heilmannii* or on the reaction of hosts (3). In this case, serum PG I/II and gastrin was within the normal range, and the histopathologic specimen showed mild gastritis. After eradication, inflammation was improved on both microscopic and macroscopic examination.

The frequency of infection of *H. heilmannii* has been reported to be much less than that of *H. pylori*. Some authors reported 0.07% (25), 0.2% (14), 0.3% (3), 0.5% (11, 23), of the adult patients who underwent upper gastrointestinal endoscopy, and the frequency in the pediatric population was reported to be 0.3% (16). Interestingly, two reports described mixed gastric infection by *H. heilmannii* and *H. pylori* (23, 26). In Japan, only three cases of the infection of *H. heilmannii* have been reported (7, 12, 14). Although it has a low frequency, *H. heilmannii* as well as *H. pylori* infection should be taken into consideration in patients with gastroduodenal disease and clinical symptoms. To clarify the clinico-pathological role with gastroduodenal disease and more effective eradication of this bacterium, examination of a larger patient population will be needed.

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