Diseases of the Stomach and Duodenum

Akira TERANO*, Masaya TAMANO** and Masashi YONEDA**

*Professor and Chairman, Department of Gastroenterology, Dokkyo University School of Medicine
**Lecturer, Department of Gastroenterology, Dokkyo University School of Medicine

Abstract: The topics of stomach and duodenum have been described in this report. The discovery of Helicobacter pylori was the revolutionary event in the pathogenesis, diagnosis as well as treatment of gastrointestinal diseases. The eradication of the bacteria prevented the recurrence of peptic ulcer, namely gastric and duodenal ulcer. It is reported that this bacteria may be the main cause of gastric cancer as well as malignant lymphoma. However, direct evidence of this relevance is still lacking and further genetic studies need to be conducted.

Key words: Stomach; Duodenum; Helicobacter pylori; Peptic ulcer; Gastric cancer; Malignant lymphoma

Introduction

Diseases of the upper gastrointestinal tract or, in other words, esophagus, stomach, and duodenum have undergone a remarkable transformation with the discovery of Helicobacter pylori. In particular, the treatment of peptic ulcer or gastroduodenal ulcer has become very easy and certain because recurrence of ulcers that was once thought to be inevitable can now be prevented by eradicating the bacteria.

Insurance coverage of the treatment has finally been approved in Japan, and eradication of H. pylori is becoming a common practice. However, reports on the occurrence of reflux esophagitis caused by eradication of the bacteria have started to be noticed, and this has become a serious issue concerning eradication therapy. The emergence of antibiotic-resistant bacteria is also an important problem. In addition, there are many more issues that need to be solved in the future including whether or not indications for eradication therapy should be expanded to include chronic gastritis and what kind of relationships there might be between H. pylori and stomach cancer or MALToma.

On the other hand, there have been significant developments in Japan in the area of endoscopic treatment of early gastric cancer. The recent developments are explained below.
DISEASES OF THE STOMACH AND DUODENUM

Peptic Ulcer

Although peptic ulcer is a representative disease that has tormented humankind since ancient times, the problem of the disease was mostly solved as an infection at the end of last century. It is unusual for a disease to undergo such dramatic development as in this case. Peptic ulcer has been treated as a representative disease that only occurs in humans as a result of psychosomatic factors such as stress. In fact, many artists and writers such as Soseki Natsume suffered from the disease, which has also affected their works.

While the discovery of H2-blockers and proton pump inhibitors (PPI) in the late 1970s has greatly contributed to the treatment of ulcers, the discovery of H. pylori in 1982 led to a Copernican development of its pathology and treatment. Specifically, by the new triple therapy that combines amoxycillin (AMPC), clarithromycin (CAM), and PPI, a 90% or greater eradication of H. pylori became possible. As a result, recurrence of ulcers that was once so troublesome is now prevented in nearly 100% of duodenal ulcer cases and in at least 80% of gastric ulcer cases.

Problems that now remain are how to handle H. pylori-negative ulcers and how to prevent and treat ulcers induced by NSAID (non-steroidal anti-inflammatory drugs). While the former has increased in Western countries, it has not been a significant problem in Japan. However, it may become a problem as eradication therapy for H. pylori advances.

NSAID-induced ulcers are a disease whose incidence has risen with the increased use of analgesics in this aging society, and it will probably continue to be a problem in the future. In particular, gastrointestinal tract hemorrhage caused by this disease has turned fatal in many cases, and it has become an important disease in the field of emergency medicine. As for treatment of gastrointestinal tract hemorrhage, recent advances in endoscopic treatment has been remarkable, and hemostasis is performed by endoscopic hemostasis, notably the clipping method in most cases.

Diffuse hemorrhage is also treated endoscopically by argon plasma coagulation (APC) and rarely requires surgical procedures. There is a world of difference between the present and a decade or two ago.

H. Pylori

It has been 20 years since the discovery of H. pylori. During this time, the pathology, diagnosis, and treatment of upper gastrointestinal diseases have undergone revolutionary transformation. In particular, as mentioned earlier, it can be said that treatment of peptic ulcers has been established as infection treatment. It is said that chronic gastritis, particularly atrophic gastritis, is also caused by the same type of infection. Classification of gastritis has also changed radically, and the Sydney Classification is gradually starting to be used in Japan. One problem remains with respect to whether or not atrophic glands recover after bacterial eradication, and this point is still debated among pathologists.

As for diagnostic method, microscopic examination, culture technique, and rapid urease test are commonly performed as invasive methods, i.e., endoscopic methods. As non-invasive methods, serum antibody assay and urea breath test are used, and urine antibody and feces antigen measurements have also been performed more recently.

As for bacterial eradication method, the aforementioned new triple therapy has been used across the world, and the method is now covered by the national health insurance in Japan as of November 2000. However, with regard to national health insurance coverage, problems concerning the selection of diagnostic methods, secondary eradication methods, target of eradication, and many other problems exist and await urgent settlement. In addition, there are important problems following bacterial eradication that must be solved — these
include reflux esophagitis, occurrence of cardia cancer, and emergence of resistant bacteria.

**Malignant Tumors of the Stomach and H. Pylori**

It is a well-known fact that the incidence of stomach cancer in Japan largely surpasses that in other advanced countries. One of the reasons is said to be *H. pylori* infection.

Since the WHO reported the close relationship between the bacteria and stomach cancer was similar to the relationship between cigarettes and lung cancer, there has been a greater awareness of this relationship. However, the direct causal relationship between the two has not been determined.

It is strongly believed that the role of *H. pylori* is displayed at the beginning of atrophic gastritis stage and changes from intestinal metaplasia to stomach cancer, and other elements such as nitrosamine are involved in the development of the cancer thereafter. In animal experiments, a Japanese report on how stomach cancer occurred when Mongolian gerbil had been infected with the bacteria has drawn international attention. Conversely, Uemura et al. observed people with and without *H. pylori*-infection for eight years, and reported in *the New England Journal of Medicine* that stomach cancer did not occur in the latter and a statistically significant difference was noted between the two groups (Fig. 1). This problem remains inconclusive until the results of the intervention study conducted by the cancer center in Japan are reported.

In contrast, data about the pathogenicity of *H. pylori* were recently published in *Science* by Higashi et al. and have drawn attention. Although CagA, a cytotoxin of *H. pylori*, has attracted some interest for quite some time, Higashi et al. reported that CagA is injected into epithelial cells when *H. pylori* attaches to the cells, affecting cell proliferation and motility through a phosphorylation process. This information may be very important for elucidation of the causal relationship between stomach cancer and *H. pylori*.

Concerning the relationship between malignant tumors of the stomach and *H. pylori*, an important point is the so called low-malignancy MALToma, a type of malignant lymphoma of the stomach, which has been found to disappear when bacterial eradication is performed, thus making eradication the first-line therapy. Of course, accurate diagnosis is particularly important in this case, and it should be made carefully in cooperation with pathologists.

Recent developments in diseases of the stomach and duodenum were discussed above.

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pylori and reflux of gastric/esophageal reflux. 
