The Association of *H. pylori* infection and patterns of erythematous gastric mucosa

Yoshihisa Urita, Toshiyasu Watanabe, Ikutaka Takemoto, Hideki Tanaka, Naoyuki Kawagoe, Motoi Takeuchi, Kazuo Hike, Yoshiko Honda, Hitoshi Nakajima, Nagato Shimada, Motonobu Sugimoto

Department of General Medicine and Emergency Care, Toho University School of Medicine, Omori Hospital, Tokyo, Japan

Abstract

It has been uncertain what types of erythematous gastric mucosa are produced by *Helicobacter pylori* (*H. pylori*)-infection. We therefore design the present study to identify the type of erythematous mucosa associated with *H. pylori*-infection. A total of 590 consecutive Japanese patients (mean age 58.7 years, 185 men and 405 women) referred to our hospital for diagnostic upper gastrointestinal endoscopy were recruited in this study. We assessed endoscopically the type of gastric mucosal erythema, including spotty erythema, haemorrhagic erosion, reddish streaks, and raised erosion. *H. pylori* infection was diagnosed by a positive endoscopic ^{13}C-urea breath test (e-UBT). Of the 402 *H. pylori*-positive subjects, spotty erythemas in the corpus were found in 177 (44.0%), haemorrhagic erosions in 26 (6.5%), reddish streaks in the antrum in 21 (5.2%) and in the corpus in 10 (2.5%), and raised erosions in the antrum in 58 (14.4%) and in the corpus in 4 (1.0%). For spotty erythema in the upper body, sensitivity was 44.0%, specificity was 92.6% for *H. pylori* infection. Seventy-two (86.7%) of 83 patients with antral reddish streaks and 65 (52.8%) of 123 patients with antral raised erosions had *H. pylori*-negative e-UBT. Spotty erythema in the corpus was one of most frequent endoscopic findings reflecting *H. pylori* infection. In contrast, antral reddish streaks and raised erosions were likely to indicate the absence of *H. pylori*.

Introduction

Mucosal erythema is the most commonly endoscopic finding in the stomach, and the observations of erythematous mucosa may be defined endoscopically as gastritis despite a lack of evidence supporting a correlation between these endoscopic features and histologic gastritis.[1] Many investigators have described a close association between *H. pylori* infection and chronic active gastritis.[2-4] It was reported that, in *H. pylori*-infected patients with acute gastritis, endoscopy may reveal only mild erythema,[5] or hyperemic mucosa with swollen folds and erosions maximal in the antrum.[6] Although, in chronic gastritis, endoscopic findings, including antral nodularity[7,8] and large gastric folds,[9,10] have been suggested to be a sign of *H. pylori* infection, it is uncertain what type of erythematous mucosa is produced by *H. pylori*-infection. It remains, likewise, controversial whether *H. pylori*-infected gastritis can be diagnosed simply by endoscopic observation without the need for biopsies. Okusa *et al.* reported that endoscopic features associated with *H. pylori* were a vascular pattern, edema, rugal hypertrophy, nodularity, rugal atrophy, erythema with reddish streaks. Mucosa with flat erosions, and exudates were not features with *H. pylori* infection.[11] We therefore designed this study to identify the type of erythematous mucosa associated with *H. pylori* infection.

Patients and Methods

Patients

A total of 590 consecutive patients (mean age 58.7 years (19-85), M/F=185/405) referred to our hospital for diagnostic upper gastrointestinal endoscopy were recruited in this study. Exclusion criteria included the following: a history of gastrointestinal surgery, peptic ulcer disease diagnosed endoscopically; use of PPI, H2-receptor antagonist, antibiotics, steroids, or nonsteroidal anti-inflammatory drugs for a period of at least two month before the investigation.

Endoscopy

Endoscopy was performed with a Fujinon EG-410HR endoscope (Fujinon Inc. Omiya, Japan) after local anesthesia of the oropharynx. We assessed endoscopically only the type of erythematous mucosa because it was difficult to adequately diagnose endoscopic features such as edema, nodularity, granularity, friability, surface texture, and other color of mucosa. Out of various endoscopic findings, a vascular pattern, edema, rugal hypertrophy, nodularity, and rugal atrophy were not assessed in the present study because we were unable to adequately define these criteria and develop consensus regarding their appearance. In contrast, it is easy to observe endoscopic findings such as spotty erythema (Figure 1), haemorrhagic erosions (Figure 2), reddish streaks (Figure 3), and raised erosions (Figure 4), which has been frequently labeled

Correspondence: Yoshihisa Urita, Department of General Medicine and Emergency Care, Toho University School of Medicine, Omori Hospital, 6-11-1, Omori-Nishi, Ota-Ku, Tokyo 143-8541, Japan.
Tel +81.3.3762.4151 - Fax +81.3.3765.6518.
E-mail: foo@eb.mbn.or.jp

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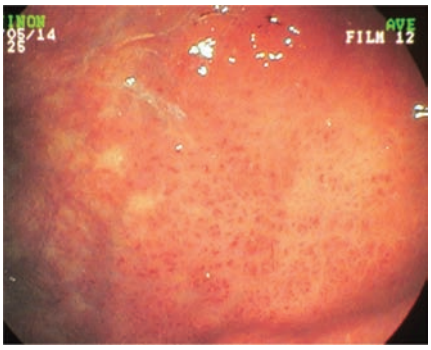

Figure 1. Endoscopic finding showing spotty erythemas in the coupus.

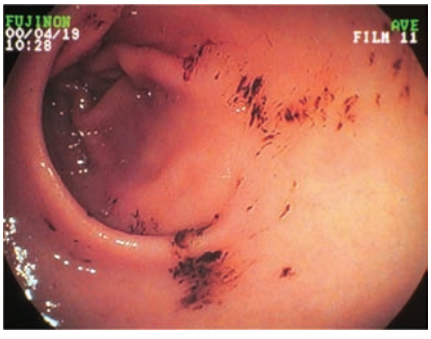

Figure 2. Endoscopic finding showing haemorrhagic erosions on the greater curvature of the antrum.

as gastritis. In addition, antral erythema is often coexistent with reddish streak or raised erosions, so this finding is not assessed in this study. Two antral biopsy specimens were taken from within 3 cm of the pylorus. One biopsy was placed in a rapid urease test (Pyloritek test, Serim Research Corp., Elkhart, IN), the other biopsy specimen was placed in 10% buffered formalin fixative for routine processing, sectioning, and staining with hematoxylin and eosin and Giemsa stains. At least one experienced histopathologist, who was blinded to endoscopic findings, evaluated the specimens. *H. pylori* was determined by Giemsa-staining sections.

Establishment of *H. pylori* status

All patients underwent the e-UBT which was described in our previous report.[12] Briefly, at the time of endoscopy, 20 mL of water containing 100 mg of ^{13}C-urea was sprayed onto the entire gastric mucosa with a spraying instrument and after that, a gastric gas sample, a volume of 150 mL, was collected through the biopsy channel. ^{13}C was measured as the $^{13}CO2/^{12}CO2$ isotope ratio and expressed as Δ over baseline (‰). Breath samples were analyzed with a mass spectrometry. A change of the Δ^{13}C value over baseline of more than 10‰ was considered positive.

H. pylori IgG antibody concentrations in the serum were measured with an ELISA method (HM-CAP).[13] A value of >2.2 was considered positive and a value of <1.9 was considered negative. Patients with a value of between 1.9 and 2.2 were excluded in this study.

A patient was considered to be infected with *H. pylori* when at least two of the three applied invasive methods (e-UBT, rapid urease test, and histology) were postive and considered to be noninfected when all of the tests, including serology, were negative. Patients who did not fulfill these criteria were excluded from the analysis.

Statistical analysis

The EXCEL 98 program (Japanese edition, Microsoft, Inc., USA) was used for statistical analysis of data. To determine whether the prevalence frequency of endoscopic features is independent of *H. pylori* infection, the Fisher's exact test was used. Odds ratios for endoscopic features were calculated by multivariate logistic regression analysis to assess the strength of associations between endoscopic features and *H. pylori* infection. A P value of <0.05 was considered statistically significant.

Results

On the basis of e-UBT, 402 (68.1%) patients had a positive result. Patients with a negative result of e-UBT but positive or intermediate results in serology were not enrolled into the study. Of the 402 *H. pylori*-positive subjects, spotty erythematous mucosa in the corpus was the more frequently endoscopic feature in 177 patients (44.0%), following by haemorrhagic erosions in 26 (6.5%), reddish streaks in the antrum in 21 (5.2%) in the corpus in 10

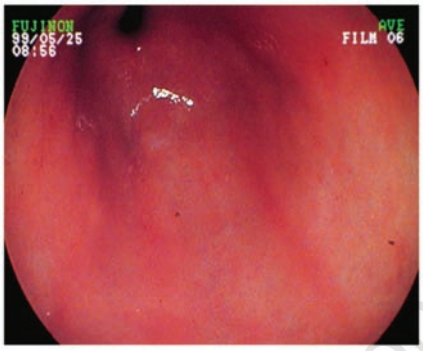

Figure 3. Endoscopic finding showing reddish streaks on the greater curvature of the antrum.

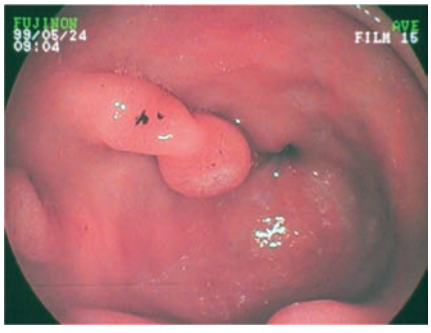

Figure 4. Endoscopic finding showing a raised erosion in the antrum.

Table 1. Number of patients with the different endoscopic features of *H.pylori*-positive and -negative gastritis.

Endoscopic features	*H. pylori*-positive	*H. pylori*-negative
No. of patients	402	188
Spotty erythema (Corpus)	177 (44.0%)*	14 (7.4%)
Reddish streaks		
Antrum	21 (5.2%)	72 (38.3%)*
Corpus	10 (2.5%)	10 (5.3%)
Raised erosions		
Antrum	58 (14.4%)	65 (34.6%)*
Corpus	4 (1.0%)	3 (1.6%)
Haemorrhagic erosions	26 (6.5%)	39 (20.7%)*

*P<0.001

Table 2. Sensitivities, specificities, positive predictive values, and negative predictive values of each feature for *H. pylori* infection.

Endoscopic features	Sensitivity	Specificity	PPV	NPV
Spotty erythema (Corpus)	44.0%	92.6%	92.7%	43.6%
Reddish streaks				
Antrum	5.2%	61.7%	22.6%	23.3%
Corpus	2.5%	4.7%	50.0%	31.2%
Raised erosions				
Antrum	4.4%	65.4%	7.2%	26.3%
Corpus	1.0%	98.4%	57.1%	31.7%
Haemorrhagic erosions	6.5%	9.3%	40.0%	28.4%

Table 3. Odds ratios calculated by multivariate logistic regression analysis to assess the strength of associations between endoscopic features and *H. pylori* infection.

Endoscopic features	Odds ratio	95%
Spotty erythema (Corpus)	9.80	5.5-17.4
Reddish streaks		
Antrum	0.09	0.05-0.15
Corpus	0.45	0.19-1.11
Raised erosions		
Antrum	0.32	0.21-0.48
Corpus	0.62	0.14-2.80
Haemorrhagic erosions	0.26	0.15-0.45

(2.5%), raised erosions in the antrum in 58 (14.4%) and in the corpus in 4 (1.0%). The sensitivity, specificity, positive predictive value, and negative predictive value of each finding are shown in Table 1. Spotty erythematous mucosa in the corpus was the noticeable finding observed in *H. pylori*-positive patients which was a more frequent finding than other findings. For spotty erythematous mucosa in the corpus, sensitivity was 44.0%, specificity was 92.6%, positive predictive value was 92.7%, and negative predictive value was 43.6% for *H. pylori* infection.

Both antral reddish streaks and antral raised erosions were the most frequently endoscopic features *H. pylori* negative patients (72 of 188, 61.7%) of 188. Seventy-two (86.7%) of 83 patients with antral reddish streaks and 65 (52.8%) of 123 with antral raised erosions were decided as *H. pylori*-negative by e-UBT. Haemorrhagic erosions were also found in more of *H. pylori*-negative patients. With respect to reddish streaks and raised erosions in the corpus, there was no significant difference between patients with and without *H. pylori* infection. The odds ratios for reddish streaks, raised erosion, and haemorrhagic erosion were under 1.0. These results suggested that erythematous mucosa in the corpus is the most frequent endoscopic feature associated with *H. pylori* infection.

Discussion

H. pylori infection is believed to be contracted mainly in childhood and then to persist as a chronic infection throughout life.[14,15] *H. pylori* infection results in acute or chronic gastritis.[16] Long-term infection may induce progression from inflammation to gastric atrophy and subsequently to intestinal metaplasia.[17,18] These inflammatory changes may cause the superficial change in color of the gastric mucosa. With respect to local endoscopic findings such as erythema, erosion, or haemorrhage, despite the findings were easily seen by routine upper gastrointestinal endoscopy, it was reported by Sauerbruch T *et al.*[19] and Laine L *et al.*[20] that interobservers' agreement was often poor. These may result from lack of recognition of the definition of endoscopic features between two endoscopists. Then, to avoid the disagreement and oversight, we assess only four findings, which are easily detected by endoscopists, such as spotty erythema, reddish streaks, raised erosions, and haemorrhagic erosions in this study.

It has remained controversial whether *H. pylori*-infected gastritis can be diagnosed by routine gastrointestinal endoscopy without the need for biopsies or dye-spraying methods. Okusa T *et al.*[11] studied that what endoscopic changes were a sign of *H. pylori* infection according to the modified Sydney system. Among the endoscopic criteria of the modified Sydney system, endoscopic features associated with *H. pylori* were a vascular pattern, edema, rugal hypertrophy, nodularity, rugal atrophy, erythema with reddish streaks excluded, flat erosions, and exudate.[11] Out of these endoscopic findings, a vascular pattern, edema, rugal hypertrophy, nodularity, and rugal atrophy were not assessed in our study because we were unable to adequately define these criteria and develop consensus regarding their appearance. In addition, since antral erythema is often coexistent with other types of erythema such as reddish streak or raised erosions, we cannot classify such erythema definitely. Then antral spotty erythema is not assessed in this study.

In this study, spotty erythemas in the corpus were found in 177 (44.0%) of 402 *H. pylori*-positive patients. If the findings are observed at endoscopy, the patient should have *H. pylori*-infected gastritis in the ratio of 92.7%. Although sensitivity was only 44.0%, specificity and positive predictive value was above 92%. These results indicate that we have to pay our attention to the presence of spotty erythemas in the corpus when endoscopy is performed in patients probably infected with *H. pylori*.

In contrast, the odds ratios for mucosal erythemas other than spotty erythema were under 1.0. Among these erythemas, the odds ratio for reddish streaks in the antrum was the minimum one. Out of 93 patients with reddish streaks, 72 (77.6%) had *H. pylori*-negative results by e-UBT. Raised erosions were also easily identified at endoscopy. Khakoo SI *et al.*[21] reported that raised erosions were associated with *H. pylori* infected gastritis, whereas Ohkusa T *et al.*[11] and Bah A *et al.*[22] described that this endoscopic finding had no definite relation to *H. pylori* infection. In our study, the detection rates of raised erosions in the antrum and the corpus were higher in *H. pylori*-negative patients than in *H. pylori*-positive ones. Similarly, the odds ratio for haemorrhagic erosions was lower in *H. pylori*-negative patients, suggesting that this endoscopic feature is not associated with *H. pylori* infection but with other factors, such as acid secretion or motility disorders.

Recently many Japanese companies adopt an endoscopic examination as the first screening step for the early detection of the gastric cancer.

Then it is a two-bird-one-stone solution that *H. pylori* infection is diagnosed by screening endoscopy because persistent infection with *H. pylori* is now accepted as being a major risk factor for the development of gastric carcinoma.[22-24] From these view points, the endoscopic feature, including spotty erythema in the corpus, with high specificity and positive predictive value for *H. pylori* infection should be identified at the time of endoscopy.

In conclusion, spotty erythema in the corpus was closely associated with *H. pylori* infection. In contrast, antral reddish streaks and raised erosions were less likely associated with *H. pylori*. Thus, *H. pylori*-infected gastritis may be probably diagnosed on the basis of the presence or absence of various types of erythema observed on a routine endoscopic examination.

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