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Retrospective Study

Mucosal patterns change after *Helicobacter pylori* eradication: Evaluation using blue laser imaging in patients with atrophic gastritis

Nishikawa Y *et al.* Mucosal patterns change after *H. pylori* eradication

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Abstract

BACKGROUND

Mucosal patterns (MPs) observed on blue laser imaging in patients with atrophic gastritis can be classified as spotty, cracked, and mottled. Furthermore, we hypothesized that the spotty pattern may change to the cracked pattern after *Helicobacter pylori* (*H. pylori*) eradication.

AIM

To further substantiate and comprehensively investigate MP changes after *H. pylori* eradication in a larger number of patients.

METHODS

We included 768 patients who were diagnosed with atrophic gastritis with evaluable MP using upper gastrointestinal endoscopy at the Nishikawa Gastrointestinal Clinic, Japan. Among them, 325 patients were *H. pylori*-positive, and of them, 101 patients who underwent upper gastrointestinal endoscopy before and after *H. pylori* eradication were evaluated for post-eradication MP changes. The patients' MPs were interpreted by three experienced endoscopists who were blinded to their clinical features.

RESULTS

Among 76 patients with the spotty pattern before or after *H. pylori* eradication, the pattern disappeared or decreased in 67 patients [88.2%, 95% confidence interval (CI): 79.0%-93.6%), appeared or increased in 8 patients (10.5%, 95%CI: 5.4%-19.4%), and showed no change in 1 patient (1.3%, 95%CI: 0.2%-7.1%). In 90 patients with the cracked pattern before or after *H. pylori* eradication, the pattern disappeared or decreased in 7 patients (7.8%, 95%CI: 3.8%-15.2%), appeared or increased in 79 patients (87.8%, 95%CI: 79.4%-93.0%), and showed no change in 4 patients (4.4%, 95%CI: 1.7%-10.9%). In 70 patients with the mottled pattern before or after *H. pylori* eradication, the pattern disappeared or decreased in 28 patients (40.0%, 95%CI: 29.3%-51.7%), appeared or

increased in 35 patients (50.0%, 95%CI: 38.6%-61.4%), and showed no change in 7 patients (10.0%, 95%CI: 4.9%-19.2%).

CONCLUSION

After *H. pylori* eradication, MPs changed from spotty to cracked in most patients, which may help endoscopists easily and precisely evaluate *H. pylori*-related gastritis status.

Key Words: Atrophic gastritis; *Helicobacter pylori*; Gastrointestinal endoscopy; Image enhancement; Classification

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Core Tip: We investigated whether the mucosal patterns on blue laser imaging may change from spotty to cracked after *Helicobacter pylori* (*H. pylori*) eradication. The spotty pattern disappeared or decreased in 88.2% of patients, while the cracked pattern appeared or increased in 87.8% of patients. These suggest that the spotty pattern observed in *H. pylori*-positive patients is likely to disappear after eradication and may be replaced by the cracked pattern. These observations may help endoscopists easily and precisely evaluate *H. pylori*-related gastritis status.

INTRODUCTION

Helicobacter pylori (*H. pylori*) infection and related atrophic gastritis is closely associated with the development of gastric cancer^[1]. Therefore, it is critical to observe the gastric mucosa to precisely judge the infection status as “current,” “previous,” or “none.” Recently, various types of image-enhanced endoscopy have been used to ensure the accurate evaluation of *H. pylori* infection^[2-6].

In our previous study^[7], we classified mucosal patterns (MPs) into three types (spotty, cracked, and mottled) using blue laser imaging (BLI)^[8,9] in patients with *H. pylori*-related gastritis. We found that the spotty pattern indicated the possibility of *H. pylori* infection, the cracked pattern indicated a post-inflammatory change after *H. pylori* eradication, and the mottled pattern indicated an intestinal metaplasia resulting from the progression of *H. pylori*-related gastritis. Thus, we hypothesized that the spotty pattern would disappear or decrease and the cracked pattern would newly appear or increase after *H. pylori* eradication.

To further explore these changes, we quantitatively analyzed the changes to determine whether each pattern would increase, decrease, or remain unchanged. Since little is known concerning the pattern changes after *H. pylori* eradication, clarification of these changes may help endoscopists diagnose the existing pattern as being pre- or post-eradication and understand the MP changes more precisely. Thus, this study aimed to clarify the significance and diagnostic viability of each MP using BLI.

MATERIALS AND METHODS

Patients and methods

A total of 2242 patients underwent upper gastrointestinal (GI) endoscopy at the Nishikawa Gastrointestinal Clinic, Ehime, Japan from April 1, 2015 to March 31, 2017. Of these, 768 patients were endoscopically diagnosed with atrophic gastritis. The presence or absence of *H. pylori* infection was confirmed. Among them, 325 patients were *H. pylori*-positive, and of them, 101 patients who underwent *H. pylori* eradication and subsequent endoscopy were examined for MP changes.

An EG-L580NW nasal upper GI endoscope (FUJIFILM Medical Co. Ltd., Tokyo, Japan) was used orally or nasally. The BLI bright mode was used to evaluate MPs in the intermediate or distant views.

This study was approved by the Ethics Committee of Ehime University Hospital (No: 1605010; August 22, 2016). Prior to receiving an endoscopic examination, all patients agreed that the data obtained in this study might be published in academic papers.

Classification of MPs

The MPs were classified into three types: the spotty pattern, which consists of 1-2 mm diameter spots (Figure 1); the cracked pattern, which consists of net-like cracks (Figure 2); and the mottled pattern, which has a mottled appearance (Figure 3)^[7].

Evaluation of the MP changes after *H. pylori* eradication

The MP patterns were evaluated as follows: (1) Three expert GI endoscopists, with at least 25 years of experience, evaluated the mucosal changes after *H. pylori* eradication; (2) They were blinded to the patients' endoscopic data, including the patterns obtained before and/or after *H. pylori* eradication; (3) They compared two randomly listed endoscopic image groups and evaluated which image group was dominant, less dominant, equal, or absent for the spotty, cracked, and mottled patterns; (4) When two or all endoscopists agreed on a particular pattern, that pattern was adopted for analysis. When they had conflicting pattern determinations, the final determination was reached through a joint discussion; and (5) *H. pylori* infection was diagnosed using the anti-*H. pylori* IgG antibody serology tests^[10,11], urea breath tests^[12-15], and biopsies.

2 ***Statistical analysis***

Student's *t*-test was used for the analysis of age, and the χ^2 test was used for the analyses of other variables. Statistical significance was set at $P < 0.05$. A 95% confidence interval (CI) was calculated to determine the uncertainty of the sample estimates. All statistical analyses were performed using Microsoft Excel 2016, version 1907, Build 11901.20176 (Microsoft Corporation, Redmond, WA, United States), and the statistical methods of this study were reviewed by Dr. Natsumi Yamashita from Clinical Research Center, National Hospital Organization Shikoku Cancer Center.

RESULTS

Patient characteristics

The number of patients evaluated was 768 (480 females and 288 males) with a mean age of 65.8 ± 12.9 (standard deviation) years. The numbers of patients with and without *H. pylori* infection were 325 (204 females and 121 males) and 443 (276 females and 167 males), respectively.

The mean ages of patients with and without *H. pylori* infection were 61.6 ± 14.3 years and 68.9 ± 10.7 years, respectively, with significant differences among them ($P < 0.001$). No significant difference was observed between the proportions of female and male patients with and without *H. pylori* infection ($P = 0.895$; Table 1).

Changes in MPs after H. pylori eradication

Upper GI endoscopy was performed for 101 patients (females: 75; males: 26; mean age: 57.5 ± 14.1 years) who successfully underwent *H. pylori* eradication, and the endoscopic mucosal changes were evaluated. Patients in whom evaluation was difficult because there were no comparable images of the specific parts were excluded from the analysis. The mean interval between *H. pylori* eradication and post-eradication endoscopy was 27.1 ± 13.1 mo.

In our study, multiple patterns commonly coexisted in many patients, with some patients having all three patterns. Of the 101 patients, 38 patients showed all three patterns (spotty, cracked, and mottled), 59 had two patterns (spotty and cracked, 28; spotty and mottled, 7; and cracked and mottled, 24), and 4 patients presented with only one pattern (spotty, 3; cracked, 0; and mottled, 1) either before or after eradication.

In 76 patients with a spotty pattern before or after *H. pylori* eradication, the pattern disappeared or decreased in 67 patients (88.2%, 95%CI: 79.0%-93.6%) and appeared or increased in 8 patients (10.5%, 95%CI: 5.4%-19.4%). In 1 patient (1.3%, 95%CI: 0.2%-7.1%), no change was observed after *H. pylori* eradication.

In 90 patients with a cracked pattern before or after *H. pylori* eradication, the pattern disappeared or decreased in 7 patients (7.8%, 95%CI: 3.8%-15.2%) and appeared or increased in 79 patients (87.8%, 95%CI: 79.4%-93.0%). In 4 patients (4.4%, 95%CI: 1.7%-10.9%), no change was observed after *H. pylori* eradication.

In 70 patients with a mottled pattern before or after *H. pylori* eradication, the pattern disappeared or decreased in 28 patients (40.0%, 95%CI: 29.3%-51.7%) and appeared or increased in 35 patients (50.0%, 95%CI: 38.6%-61.4%). In 7 patients (10.0%, 95%CI: 4.9%-19.2%), no change was observed after *H. pylori* eradication (Figure 4).

We investigated the relationship between the spotty and cracked patterns before and after eradication. The spotty pattern disappeared or decreased in 67 out of the 76 patients who had a spotty pattern before or after eradication. Of the 67 patients, the cracked pattern appeared or increased in 55 patients. Among the 8 patients with spotty patterns that appeared or increased after eradication, the cracked pattern appeared or increased in 5 patients. The cracked pattern appeared or increased in most of the 25 patients who did not have a spotty pattern before or after eradication (Figure 5).

We further investigated the difference in MP changes due to *H. pylori* eradication between the short-term (8-24 mo) and long-term (25-60 mo) observation groups. The spotty pattern disappeared or decreased in 88.6% and 87.8% (short-term *vs* long-term) of the patients. The cracked pattern newly appeared or increased in 88.9% and 86.7% (short-term *vs* long-term) of the patients. No significant differences were observed between the patients under short-term and long-term observations.

DISCUSSION

We investigated the use of BLI, an image-enhanced endoscopy, for the diagnosis of *H. pylori*-related gastritis, with a focus on the MP changes after *H. pylori* eradication. The Kyoto Classification of Gastritis was established in 2014 for the endoscopic diagnosis of *H. pylori*-related gastritis^[16,17]. The classification of MPs observed on BLI in this study is simpler and easier to use in endoscopic assessment than the Kyoto classification and thus has the potential to become a new standard method with the addition of new diagnostic information to the Kyoto classification. We previously reported the efficacy of MPs on BLI in an intermediate-to-distant view evaluation of *H. pylori* infection and had the benefits of easy detection of atrophic gastritis and easy diagnosis of infection status (current, previous, or no infection)^[7].

The results obtained in the current study indicate that the disappearance of the spotty pattern is evidence of *H. pylori* clearance, while newly-appearing cracked pattern is evidence of post-gastritis healing. The mottled pattern may reflect “intestinal metaplasia,” as identified in our previous study using biopsies.

Knowledge of the endoscopic changes after *H. pylori* eradication is helpful in clarifying the meaning of each MP. The spotty pattern disappeared or decreased in 88.2% of patients, whereas the cracked pattern appeared or increased in 87.8% of patients after *H. pylori* eradication. The mottled pattern exhibited no specific tendency. As indicated in Figure 5, the spotty pattern observed in *H. pylori*-positive patients before eradication may disappear and may be replaced by the cracked pattern. Based on these observations, we can diagnose the *H. pylori* infection status as current, previous, or no infection. No difference was detected between the short-term and long-term observations of MP changes after *H. pylori* eradication, suggesting that the changes in MP would occur relatively quickly after eradication. The primary tendency of MP changes after *H. pylori* eradication have been clarified in this study. Irregular pattern changes (those other than spotty to cracked pattern) were observed after eradication in a limited number of patients. Further verification is necessary.

CONCLUSION

In conclusion, the spotty pattern may indicate *H. pylori* infection, ¹ the cracked pattern may indicate post-inflammatory changes after *H. pylori* eradication, and the mottled pattern may indicate intestinal metaplasia resulting from the progression of *H. pylori*-related gastritis. We verified that MPs on BLI may change from a spotty to a cracked pattern after *H. pylori* eradication. These observations may help endoscopists easily and precisely evaluate the status of *H. pylori*-related gastritis. We hope that MP changes on BLI will be routinely used to confirm the diagnosis of *H. pylori*-related gastritis in the future.

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