In vivo histopathology using endocytoscopy for non-neoplastic changes in the gastric mucosa: a prospective pilot study (with video)

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Background: Endocytoscopy (EC), as a novel ultrahigh magnification technology, enables in vivo histopathological diagnoses of the GI tract. EC is particularly exceptional when comparing dysplastic and neoplastic tissue with normal tissue. There are, however, no detailed data for minute or minimal changes in the gastric mucosa.

Objective: To describe non-neoplastic EC patterns of the gastric mucosa correlated with histopathological findings and to determine any relationship with *Helicobacter pylori* (HP) infection.

Design: A pilot prospective study.

Setting: Tertiary care referral center.

Patients: Sixty-four participants undergoing upper endoscopy for various indications.

Methods: Antral mucosal patterns on EC were divided into 4 categories: type 1 (normal), each papilla/pit has round smooth structure; type 2 (gastritis), extended, notched, and distorted structure with some necrotic tissue; type 3(atrophy), neighboring papilla/pit take on a lobulated appearance; type 4 (intestinal metaplasia [IM]), goblet cells are identified in a completely stained crypt. Target biopsy specimens were obtained from the region identified with these patterns, and multiple HP tests were performed.

Results: HP positivity was 0%, 40.9%, 50.0%, and 58.3% in types 1, 2, 3, and 4, respectively. The sensitivity and specificity of types 2+3+4 for HP positivity were 100% and 42.5%, respectively. The positive predictive values of type 1 for normal, type 2 for chronic gastritis, type 3 for atrophic gastritis, and type 4 for IM were 100%, 62.5%, 40.0%, and 100%, respectively. The sensitivity and specificity of types 3+4 for atrophic gastritis to IM were 87.0% and 95.1%, respectively.

Limitations: Small, single-center, pilot study.

Conclusions: EC can differentiate gastric mucosal patterns of minimal, non-neoplastic change and appears to reliably exclude HP infection. (Gastrointest Endosc 2015;81:875-81.)

Abbreviations: EC, endocytoscopy; HP, Helicobacter pylori; NBI, narrow-band imaging; IM, intestinal metaplasia.

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Gastric atrophy has a known association with *Helicobacter pylori* (HP) infection,[1,2] as a significant risk factor for gastric carcinoma.[3,4] In general, atrophic gastritis is diagnosed by conventional endoscopy and biopsy, whereas the detection of HP infection requires histology or some other test (rapid urease test, serum pepsinogens, urea breath test).

The endoscopic features of HP-associated gastritis are not specific as those of erythema, edema, and erosion[5,6] and therefore are difficult to distinguish from non-HP gastritis. In differentiating normal mucosa from HP gastritis, Yagi et al[7,8] reported the regular arrangement of collecting venules as a practical marker. Narrow-band imaging (NBI) with magnification appears to work well in assisting this differentiation by examining pit and microvessel pattern.[9-12]

Endocytoscopy (EC), which uses ultramagnifying endoscopy, approximates an in vivo histopathological diagnosis for the GI tract,[13] with proven efficacy in differentiating neoplastic from non-neoplastic tissue.[14-19]

It should be also possible to use EC to differentiate between non-neoplastic minimal or minute changes, but at present, there are no detailed data for EC in the differentiation of normal mucosa, HP-associated gastritis, and intestinal metaplasia (IM). In Japan, HP is also most strongly associated with chronic and atrophic gastritis. It would also be of interest to determine the value of EC in detecting HP. This study was planned to define the EC patterns associated with these histopathological changes and to determine whether HP could be reliably diagnosed.

METHODS

Patients

This study was performed at Showa University Northern Yokohama Hospital, a tertiary referral center in Japan, from September through December 2013. Sixty-four patients were enrolled prospectively in this study, referred for other conditions that necessitated endoscopic examination of the upper GI tract. The participants included 20 with gastric or esophageal cancer who were referred to our hospital for endoscopic treatment, 4 with achalasia, 13 screening for GI cancer, 11 as surveillance endoscopy after endoscopic treatment, and 6 secondary complete checkup after barium radiographic examination. The other 10 participants underwent upper endoscopy to investigate abdominal symptoms. Patients who had undergone gastric surgery or who were receiving anticoagulant therapy at the time of examination were excluded from this study.

This study was approved by our institutional review board and conducted following the registration in UMIN clinical Trials Registry (UMIN000007745). Written informed consent was obtained from all subjects.

Materials: EC

All EC examinations were performed with the integrated-type endocytoscope (GIF-Y0002) (prototypes from Olympus, Tokyo, Japan). The GIF-Y0002 has 1 lens that can consecutively increase the magnification from conventional endoscopy to ×380 (tissue field of view, 700 × 600 μm), by using a hand control, thus allowing gradual magnification at the center of the monitor, ensuring that the area being viewed is located accurately. The clinical use of the prototype endoscope had also been approved by the hospital's ethics committee.

For EC, a mixture of 0.1% methylene blue and 0.05% crystal violet was used to stain the tissues and to obtain images approximating the hematoxylin and eosin histopathological stain. Cresyl violet alone effectively dyes the cytoplasm, whereas methylene blue single staining highlights details of cell structure, including nuclei and cytoplasm. The combination, in our experience, improves detailed visualization of the mucosa.

The EVIS Lucera Elite processor (Olympus) was also used. This system reduces image "noise" drastically, resulting in a sharper picture, by using a high-resolution charge-coupled device and other system developments, making it valuable for EC.

Endocytoscopic mucosal pattern

The model of previous studies of EC in the colon (Kudo et al[18]) and the esophagus (Inoue et al[14]) were used to devise endocytoscopic criteria for differentiating minimal mucosal change in the gastric mucosa. Four distinct mucosal patterns related to histological findings were identified.

Type 1. Each pit and papilla have a smooth, round structure. The crypt epithelium and its nuclei are almost unstained. None of the infiltrating cells, necrotic tissue, or debris are identified. This pattern corresponds to normal mucosa (Fig. 1A).

Type 2. The surface of the crypt epithelium is somewhat stained with an extended, notched appearance and sometimes distorted structure. Infiltrating cells and necrotic tissue are often identified. This corresponds to chronic gastritis (Fig. 1B).

Type 3. The pits/papillae become blockish or lobulated in appearance because of atrophic changes (shrinkage) with an irregular shape and size, with a more defined, distinct, and separated border and with a loss of the smooth contour seen in type 1. Infiltrating cells and necrotic tissue are often identified, but are less intense than type 2. This is atrophic gastritis (Fig. 1C).

Type 4. The lobulated appearance of the papillae seen in type 3 is apparent, perhaps with sharper margins, but now goblet cells are identified as round lucent spots in an otherwise totally stained epithelial layer. This appearance corresponds to IM (Fig. 1D).