Absent microsurface pattern is characteristic of early gastric cancer of undifferentiated type: magnifying endoscopy with narrow-band imaging

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Endoscopic submucosal dissection (ESD) for early gastric cancer (EGC), currently a standard therapy in Japan and South Korea, is being used more commonly worldwide.[1] ESD allows en bloc resection even of large lesions and is technically possible regardless of resection size. However, the risk of lymph node metastasis from EGC depends on not only the size, but also on the histological type.[2-4] Undifferentiated-type EGC (U-EGC) has a higher potential for lymph node metastasis than does differentiated-type EGC (D-EGC). Therefore, the indications for endoscopic resection of U-EGC differ from those for D-EGC.[1-4] In this context, discriminating U-EGC from D-EGC accurately is important. On endoscopic examination by using conventional white-light imaging, U-EGC tends to exhibit pale, depressed lesions with irregular margins.[5] However, such lesions are sometimes observed in patients with D-EGCs. Therefore, an additional endoscopic examination approach that allows for discrimination between U-EGC and D-EGC is necessary. Moreover, small-forceps biopsies may not be representative of the entire lesion, making accurate histological diagnosis problematic.[6]

Recently, Yao et al[7] proposed a useful diagnostic system called the "vessel plus surface classification system" in which irregular microvascular and/or irregular microsurface patterns with clear demarcation line are hallmarks of EGC. In addition, microsurface patterns characterized by marginal crypt epithelium (MCE) and white opaque substance (WOS) are reportedly found in EGCs by magnifying endoscopy with narrow-band imaging (ME-NBI).[7] Recently, we noted that these features of a microsurface pattern are generally present in D-EGCs but often absent in U-EGCs. Thus, evaluating the presence or absence of such microsurface patterns by ME-NBI may be useful for distinguishing between U-EGCs and D-EGCs. In this study, therefore, we aimed to clarify whether detection of absent microsurface pattern (AMSP) on ME-NBI examination helps to discriminate U-EGCs from D-EGCs.

METHODS

Patients

This study was based on a retrospective analysis of our endoscopic image database in Osaka Red Cross Hospital. Consecutive patients who met the following inclusion and exclusion criteria were enrolled. This study was approved by our institutional review board. Written informed consent had been obtained from all patients for the endoscopic procedures. All lesions had to be examined by ME-NBI at Osaka Red Cross Hospital from January 2010 to September 2011, endoscopically or surgically resected en bloc, and histologically diagnosed as EGC. Lesions for which only low-magnification endoscopic images had been recorded or those histologically diagnosed as mixed-type D-EGC and U-EGC were excluded from the study. As a result, 88 consecutive patients with 93 lesions (14 U-EGCs and 79 D-EGCs) were included in this study.

Endoscopic procedure

Endoscopic examinations were performed with a high-definition upper GI endoscope (GIF-H260Z; Olympus Medical Systems, Tokyo, Japan) with an electronic endoscopy system (EVIS LUCERA system; Olympus Medical Systems) by 4 experienced endoscopists (T.K., A.S., T.T., and T.M.). Before the examination, a soft hood (MB-46; Olympus Medical Systems) was mounted on the tip of the endoscope to enable the endoscopist to consistently fix the mucosa at a distance of approximately 2 mm.

Abbreviations: AMSP, absent microsurface pattern; D-EGC, differentiated-type early gastric cancer; EGC, early gastric cancer; ESD, endoscopic submucosal dissection; MCE, marginal crypt epithelium; ME-NBI, magnifying endoscopy with narrow-band imaging; ROC, receiver-operating characteristic; U-EGC, undifferentiated-type early gastric cancer; WOS, white opaque substance.

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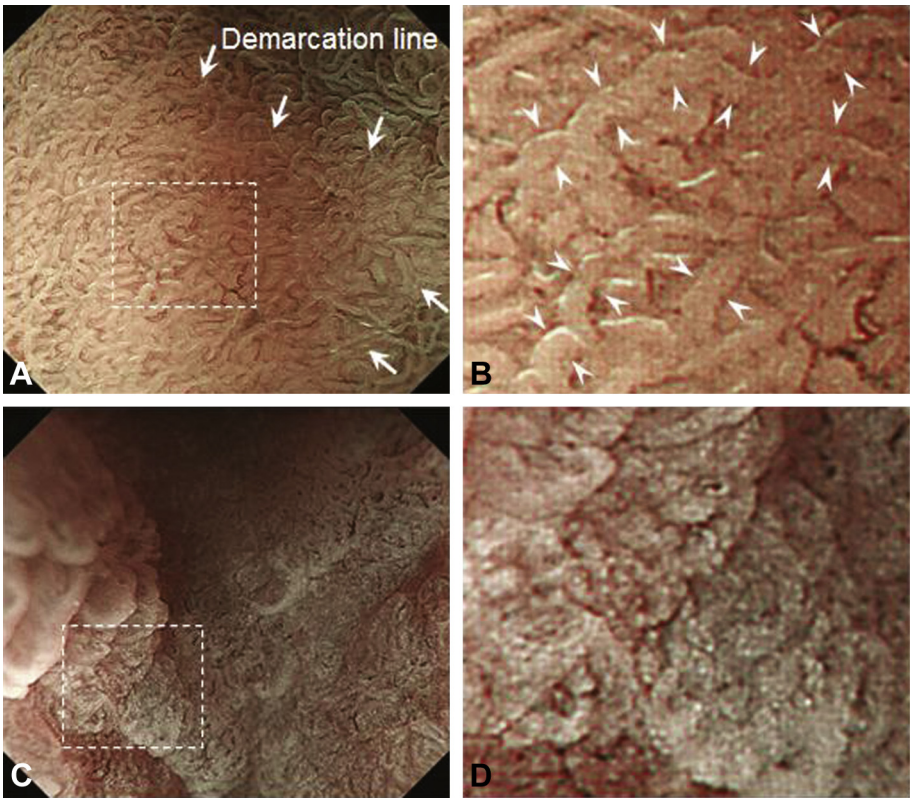

Figure 1. Representative examples of microsurface patterns. **A**, Magnifying endoscopy with narrow-band imaging (ME-NBI) feature of marginal crypt epithelium (MCE) in differentiated-type early gastric cancer (D-EGC). A demarcation line is visible at the border of the lesion as shown by *arrows*. **B**, ME-NBI of the boxed area in **A**. As indicated by the *arrowheads*, MCE is a semitransparent linear area of a constant width. A whitish sharp line is frequently observed on 1 side of the edge. **C**, ME-NBI of white opaque substance (WOS) in D-EGC. **D**, ME-NBI of the boxed area in **C**. Fine speckled WOS is visible throughout the surface of the lesion.

Maximal magnification of endoscopic images can be easily obtained by using this hood. Patients were given the following mixture 30 minutes before the endoscopic procedure: 100 mL of water with 20,000 U of pronase (Pronase MS; Kaken Pharmaceutical, Tokyo, Japan) and 10 mL of dimethylpolysiloxane (20 mg/mL; Horii Pharmaceutical Industries, Osaka, Japan). All examinations were performed with the patient under conscious sedation using 1 to 3 mg of midazolam (Dormicum; Astellas Pharma, Tokyo, Japan).

Evaluation of microsurface pattern

Previous reports had described MCE as a feature of the microsurface pattern seen on ME-NBI.[7] As shown in the region indicated by the arrowheads in Figure 1B, on ME-NBI, MCE appears as semitransparent linear areas of constant width (Figs. 1A and 1B). A whitish sharp line is frequently observed on 1 side of its periphery. Visualization of MCE by ME-NBI is caused by back-scattering of the light. On the other hand, WOS is observed as a range of white specks (Figs. 1C and 1D). Yao et al[8] and Ueo et al[9] reported that WOS represents intramucosal accumulation of lipid droplets. WOS frequently overlaps in appearance with MCE. Areas without MCE or WOS were defined as AMSP in this investigation.

The presence and proportion of AMSP areas in the entire lesions were evaluated by examining magnified endoscopic images. The optimal cutoff value for the percentage of the AMSP area for distinguishing U-EGCs from D-EGCs was then calculated by constructing a receiver-operating characteristic (ROC) curve. The sensitivity, specificity, and accuracy of the proportion of AMSP area for distinguishing U-EGCs from D-EGCs were also calculated.

Pathological diagnosis

Specimens obtained by endoscopic or surgical resection were histologically evaluated by using hematoxylin and eosin staining. Pathological diagnoses were made according to the Vienna and Japanese classifications of gastric carcinoma by 2 experienced pathologists (T.W. and M.S.). In this study, well- and moderately differentiated tubular adenocarcinomas and papillary adenocarcinomas were classified as D-EGCs and poorly differentiated adenocarcinomas and signet-ring cell carcinomas as U-EGCs. Only lesions that had been given identical diagnoses by the 2 pathologists were included in the study.