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【 CASE REPORT 】

Heterotopic Gastric Mucosa in Middle Esophagus Complicated with Esophageal Ulcers

Kenichi Kishimoto[1], Kotaro Shibagaki[2], Saya Nonomura[1], Shohei Sumi[1], Naoki Fukuda[3], Yusuke Takahashi[1], Satoshi Kotani[1], Eiko Okimoto[1], Naoki Oshima[2], Kousaku Kawashima[1], Norihisa Ishimura[1] and Shunji Ishihara[1]

Abstract:
Heterotopic gastric mucosa (HGM) of esophagus, primarily occurring in cervical esophagus, is usually asymptomatic. A healthy woman (mid-40s) with postprandial heartburn was diagnosed with middle esophageal HGM and esophageal ulcers by esophagogastroduodenoscopy. Using 8-channel pH monitoring, a sensor near the HGM area detected postprandial acid phase (pH 3-4), while areas adjacent to the proximal and distal sensors were neutral, suggesting acid secretion from the HGM. A biopsy showed fundic gland tissue expressing H^+/K^+-ATPase and pepsinogen-I. Oral vonoprazan improved the clinical symptoms and endoscopic findings. This is the first report using 8-channel pH monitoring to diagnose extremely rare middle esophageal HGM.

Key words: heterotopic gastric mucosa, esophageal ulcer, pH monitoring, acid suppressive therapy, inlet patch, potassium-competitive acid blocker

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Introduction

Heterotopic gastric mucosa (HGM) of the esophagus, also termed inlet patch, is primarily localized in the cervical esophagus and rarely seen in other esophageal areas (1, 2).

Most patients with esophageal HGM are asymptomatic, and its discovery is incidental in 1.1%-10% of adults who undergo a screening endoscopy examination (3). However, some note symptoms such as cough, sore throat, or hoarseness due to acid secretion from the area of HGM (4), although severe complications, such as esophageal ulcer, stenosis, or perforation, are rare (5-8). While acid secretion in such cases has been examined by conventional 24-h dual-channel esophageal pH monitoring (9), the precise acid phase of each esophageal site is difficult to determine using that modality.

We recently developed a novel pH sensor catheter equipped with 8 vertically arrayed pH sensors (10) and herein report a case of HGM in the middle thoracic esophagus complicated with esophageal ulcers in which the acid secretion site was accurately identified by this 8-channel pH monitoring system.

Case Report

A healthy woman in her 40s underwent a screening upper endoscopy examination. An HGM area with a diameter of about 2 cm was observed in the middle thoracic esophagus and accompanied by shallow ulcers in the adjacent mucosa (Fig. 1A). On the distal side, short segmental Barrett's esophagus was observed, along with a mild sliding hiatal hernia. Narrow-band imaging with magnification endoscopy (NBIME) for the HGM revealed a brownish area clearly demarcated from the light green squamous epithelium, and tubular microstructures were observed inside the lesion (Fig. 1B). The patient had noted the occurrence of slight postprandial heartburn for a long period and was suspected of having symptomatic esophageal HGM accompanied by esophageal ulcers.

[1]Department of Gastroenterology, Faculty of Medicine, Shimane University, Japan, [2]Department of Endoscopy, Shimane University Hospital, Japan and [3]Fukuda Clinic, Japan
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Correspondence to Dr. Kotaro Shibagaki, kotaro@med.shimane-u.ac.jp

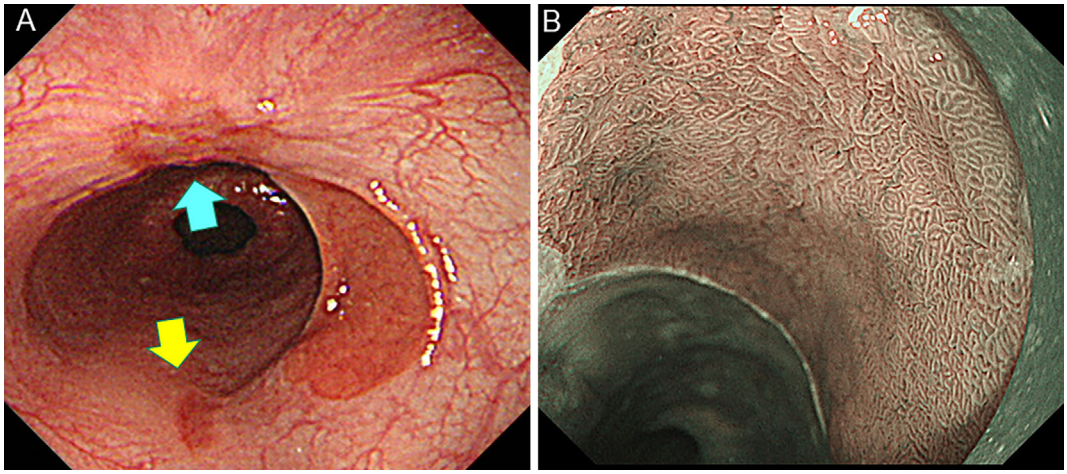

Figure 1. **Upper endoscopy findings. (A) Heterotopic gastric mucosa was observed on the right wall of the middle thoracic esophagus along with shallow ulcers in the adjacent mucosa (indicated by colored arrows). (B) Narrow-band imaging with magnification endoscopy for the HGM revealed a brownish area clearly demarcated from the light-green squamous epithelium, and tubular microstructures were observed inside the lesion.**

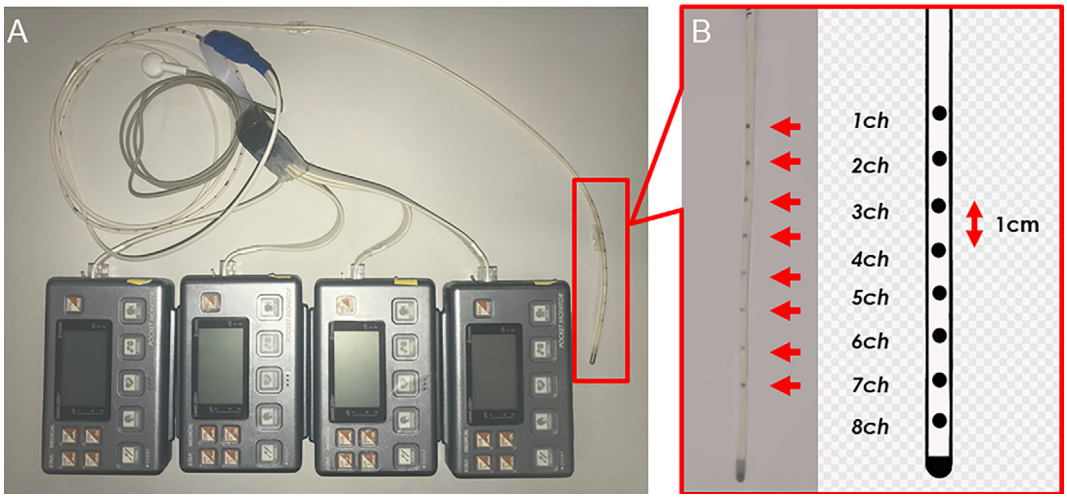

Figure 2. **Eight-channel pH sensor catheter developed in our department. (A) Four portable digital recorders are attached to the proximal end. (B) The flexible catheter measures 2.35 mm in diameter and is equipped with 8 pH electrodes along the distal end (red arrows) arranged at intervals of 1 cm on the vertical axis.**

An examination was performed using the 8-channel pH monitoring system devised by our department (10) to precisely evaluate the acid secretion from the esophageal HGM. It is equipped with a flexible catheter 2.35 mm in diameter and 8 pH electrodes along the distal end, which are arranged at intervals of 1 cm on the vertical axis, thus allowing pH to be measured over a length of 7 cm. This procedure has been approved by the ethics committee of Shimane University Hospital, and written informed consent was obtained from the patient prior to performing the procedure.

Eight-channel pH data can be simultaneously recorded by connecting the catheter to four portable digital recorders (Pocket Monitor GMMS-200pH; Star Medical, Tokyo, Japan) (Fig. 2). The catheter was inserted transnasally to position the electrodes across the HGM using fluoroscopic imaging (Fig. 3A, B) in the afternoon and remained indwelling for 15 h until its removal the following morning. The patient was not allowed to consume any acidic beverages during the examination, and her meal was that served by the hospital.

The pH monitoring showed slight acid reflux phase after the meal. The channels associated with sensors across the HGM exhibited a neutral level throughout most of the examination period. However, approximately 40 minutes after a meal, a distal-side channel temporarily exhibited an acid phase of pH 3-4 (Fig. 3C) with a minimum pH of 2.89, demonstrating acid secretion from the HGM area.

Subsequently, a biopsy sample was obtained to determine its acid-secreting capacity. The specimen was carefully

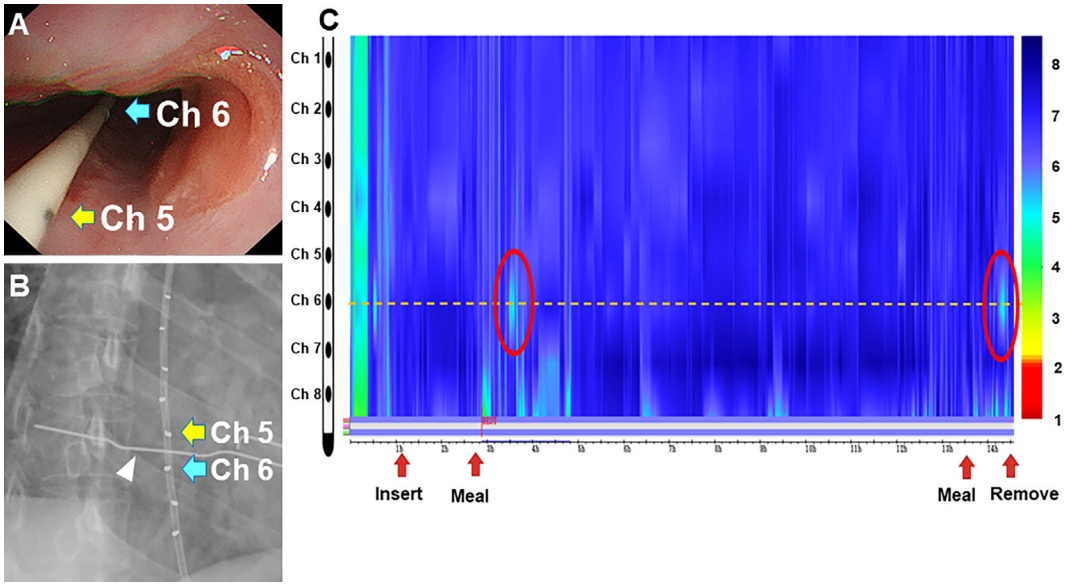

Figure 3. **(A) The pH monitoring catheter was inserted to position the heterotopic gastric mucosa between channels 5 and 6 with endoscopic observation, (B) which was also confirmed by fluoroscopy (white arrowhead indicates marker of heterotopic gastric mucosa). (C) Eight-channel pH monitoring revealed an acid phase of pH 3-4 appearing at channel 6 about 40 minutes after meals (red circles), while the adjacent proximal and distal channels exhibited a neutral level, suggesting acid secretion from the HGM area.**

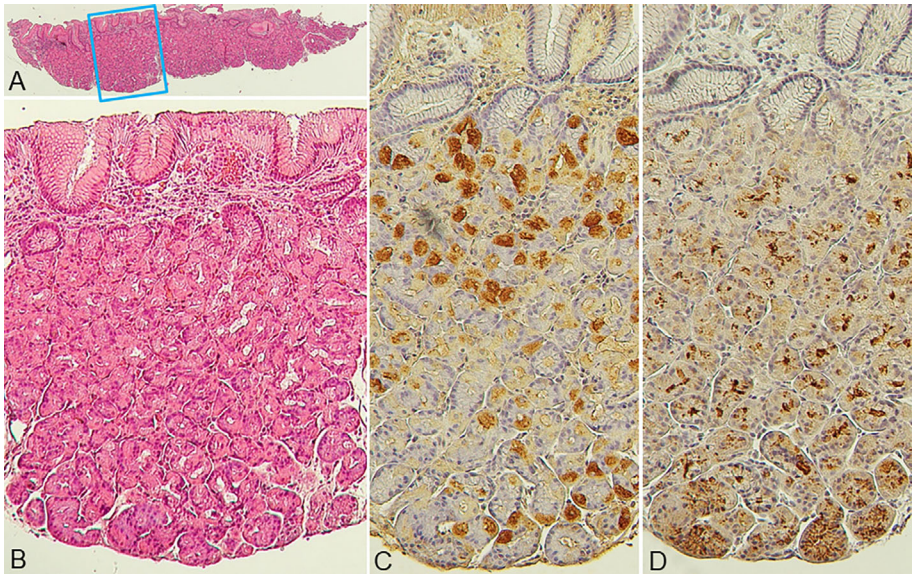

Figure 4. **Biopsy specimen. (A) The sampled tissue was satisfactorily smoothed, and a fine vertical section is shown. (B) Hematoxylin and Eosin staining demonstrated non-atrophic and little inflammatory fundic gland tissue. Immunohistochemical findings showed expression of (C) H^+/K^+-ATPase primarily in the upper layer and (D) pepsinogen-I in the lower layer, suggesting heterotopic gastric mucosa, fundic gland type.**

smoothed and attached to filter paper with the superficial side up and then subjected to formalin fixation and vertically cut on the superficial aspect. Histological results showed fine fundic gland tissue. Immunohistochemically, H^+/K^+-ATPase was expressed primarily in the upper layer of the fundic gland and pepsinogen-1 in the lower layer, suggesting fundic-gland type with acid-secreting capacity (Fig. 4). Biopsy samples were also taken from shallow ulcers found adjacent to the HGM area but showed only benign ulcer tissue with lymphocytic infiltration.

Acid suppressive therapy with the oral intake of vonoprazan was started using an initial dose of 20 mg per day for 8 weeks, followed by 10 mg per day for a longer term. After starting treatment, clinical symptoms were improved.

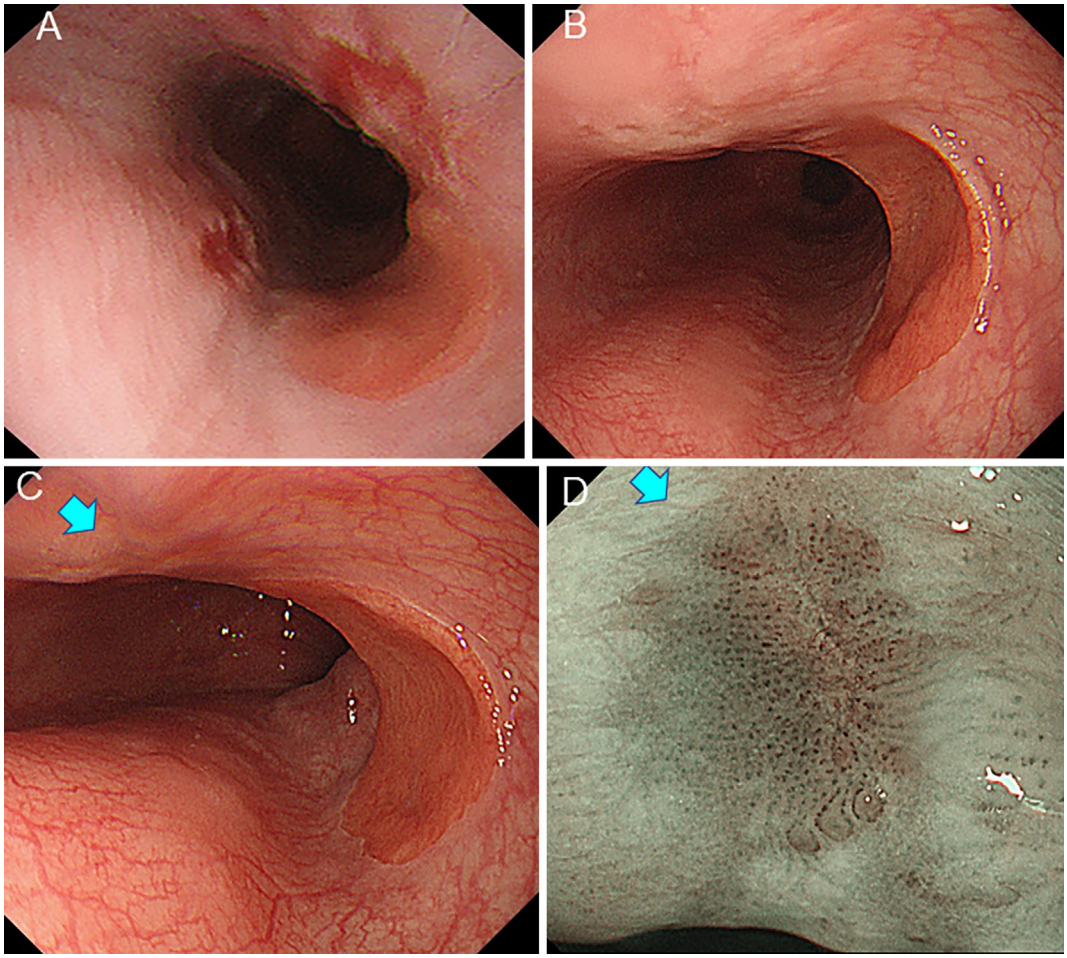

Figure 5. Endoscopic findings before and after acid suppressive therapy. (A) Shallow esophageal ulcers were noted adjacent to heterotopic gastric mucosa, and the surrounding mucosa was cloudy. (B) Following the administration of vonoprazan at 20 mg/day for 8 weeks, the ulcer was scarred, and vascular translucency improved. (C) The dosage was decreased to 10 mg, and the mucosal status was found to be well maintained 16 weeks later. (D) Narrow-band imaging with magnification endoscopy of the adjacent ulcer scar (blue arrow) showed regularly arranged, dilated intrapapillary capillary loops.

Follow-up endoscopy showed scarring of the ulcers and recovery of mucosal translucency (Fig. 5). A histologic examination of the adjacent ulcer scar revealed non-neoplastic squamous epithelium. Esophageal pH monitoring after the treatment had finished was proposed, although the patient declined.

Discussion

Esophageal squamous epithelium appears first in the middle third of the esophagus, and then extends both proximally and distally during the embryonic period. Esophageal HGM is believed to be a consequence of incomplete transformation from columnar to squamous epithelium (11) and in most cases is seen in the cervical esophagus (1, 2) or may be a pathogenic factor in the development of Barrett's esophagus (12). To our knowledge, no cases of HGM in the middle esophagus have been reported, suggesting its extremely rare incidence. We speculate that part of the middle esophagus accidentally evaded the process of replacing columnar with squamous epithelium during the embryonic period.

When a conventional dual-channel pH monitoring system is used to evaluate the acid secretion from cervical esophageal HGM, the proximal and distal sensors are placed 20 and 5 cm proximally from the lower esophageal sphincter, respectively. Acid secretion from esophageal HGM is defined as any episode of pH <4 recorded by a proximal sensor that is not preceded by an episode of pH <4 recorded by a distal sensor (3). However, this method is difficult to use to obtain precise evidence of acid secretion directly from the affected site. For the present case, we used an eight-channel pH monitoring system, and one sensor adjacent to the HGM area revealed a postprandial pH decrease, while closely adjacent proximal and distal sensors remained neutral, suggesting direct acid secretion from the area. Precise identification of the acid-secreting site is important for determining the therapeutic indication for esophageal HGM. As an alterna-

tive modality, technetium-99m (^{99m}Tc) scintigraphy is clinically applied to the detection of HGM because ^{99m}Tc has the property of accumulating in the gastric mucosa (13).

Histologically, esophageal HGM is predominantly fundic-gland type, followed by cardiac-gland type. Fundic-gland type is composed of acid-secreting parietal cells and chief cells and causes various acid-associated complications, while cardiac-type consists of cardiac gland mucosa lacking an acid-secreting ability (14). Weickert et al. investigated 33 HGM patients and classified the histologic type of HGM into oxyntic type (24%), cardiac type (15%), and mixed type (61%) (15). In the present case, a carefully treated biopsy specimen showed fine fundic gland tissue with expression of pepsinogen-I and H^+/K^+-ATPase, typical findings for fundic-gland type. We consider appropriate mucosal sampling and careful preparation to be important for the proper diagnosis of the acid-secreting capacity of HGM.

Whether or not the size of HGM is associated with patients' symptoms has been controversial in previous reports (16-18). In addition, to our knowledge, there are no reports describing the association between the location or histologic type of HGM and clinical symptoms. It is clinically difficult to accurately identify the cause of postprandial heartburn in patients with HGM. In the present case, pH monitoring revealed not only acid secretion from HGM but also slight acid reflux after a meal. We should therefore consider the possibility that gastroesophageal reflux may have also affected the patient's symptoms.

A standard treatment for esophageal HGM has yet to be established, although some case reports have described successful use of proton pump inhibitors (PPIs) for symptomatic esophageal-HGM patients (19-21). In the present case, both clinical symptom and endoscopic findings were improved following oral intake of vonoprazan, a potassium-competitive acid blocker (PCAB). Although clinical evidence is scant, oral PPI or PCAB administration is likely a safe and acceptable treatment, with a high level of reproducibility. Dunn et al. reported that radiofrequency ablation (RFA) achieved complete endoscopic and histologic resolution in 80% (8/10) of treated symptomatic esophageal-HGM patients (9). However, long-term outcomes were not demonstrated, and that treatment is not covered by health insurance in some regions, including Japan. Argon plasma coagulation and endoscopic resection (ER) are also presented as treatment options for esophageal HGM accompanying carcinoma. Small, symptomatic HGM may also be a good indication for ER. However, in the present case, as the HGM was accompanied by an ulcer in the adjacent mucosa, ER was not likely to be easy to perform. Considering the patient's mild symptoms and potential complication of ER, we considered pharmacotherapy more acceptable than ER in clinical practice.

In conclusion, we reported a case of esophageal HGM in the middle thoracic esophagus that caused esophageal ulceration in the adjacent mucosa. The eight-channel pH monitoring system employed in this case may be useful for determining the morbid state of symptomatic esophageal HGM patients.

The authors state that they have no Conflict of Interest (COI).

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