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Case Report

Curative Endoscopic Resection of a Widespread Superficial Adenocarcinoma in a Long-segment Barrett's Esophagus

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Summary

We report about a patient with an extremely rare long-segment Barrett's esophagus (LSBE) who developed extensive superficial adenocarcinoma and underwent radical (R0) resection based on an accurate preoperative diagnosis of tumor extent. A 68-year-old man with no subjective symptoms and no noteworthy medical history was diagnosed with adenocarcinoma after a biopsy of a protruding lesion in the lower esophagus. Narrow-band imaging (NBI) magnification endoscopy revealed that the protruded lesion was within the LSBE, and a flatly extended superficial esophageal adenocarcinoma (SEAC) was observed proximal to the protruded lesion. After confirming the extent of the tumorous lesion via endoscopic biopsy, subcircumferential endoscopic submucosal dissection (ESD) was performed for the extensive tumor, which resulted in a histological R0 resection. Prophylactic steroid therapy was performed to prevent refractory post-ESD stenosis. There was no residual tumor or recurrence of the cancer, and the patient's postoperative course was favorable. Preoperative diagnosis of tumor extent using NBI magnification endoscopy may therefore be useful for characterizing SEAC occurring in the LSBE, given that detecting the presence and determining the extent of these tumors is normally difficult. Prophylactic therapy with local steroid injection can prevent refractory stenosis after quite extensive ESDs for SEACs in the LSBE.

Key Words: Adenocarcinoma, Endoscopic submucosal dissection, Long-segment Barrett's esophagus, Narrow-band imaging, magnification endoscopy

Introduction

We report about a patient with an extensive superficial adenocarcinoma that arose in an extremely rare long-segment Barrett's esophagus (LSBE) and was successfully treated with endoscopic radical (R0) resection after accurate preoperative diagnosis by narrow-band imaging (NBI) magnification endoscopy.

Esophageal adenocarcinoma (EAC) arises primarily in Barrett's esophagus (BE) and is caused by gastroesophageal reflux disease (GERD)[1)]. Although EAC is one of the most common malignancies in Western countries[2)], it is considered rare in Japan. However, with the increase in the incidence of GERD owing to the Westernization of diet and the decrease in the rate

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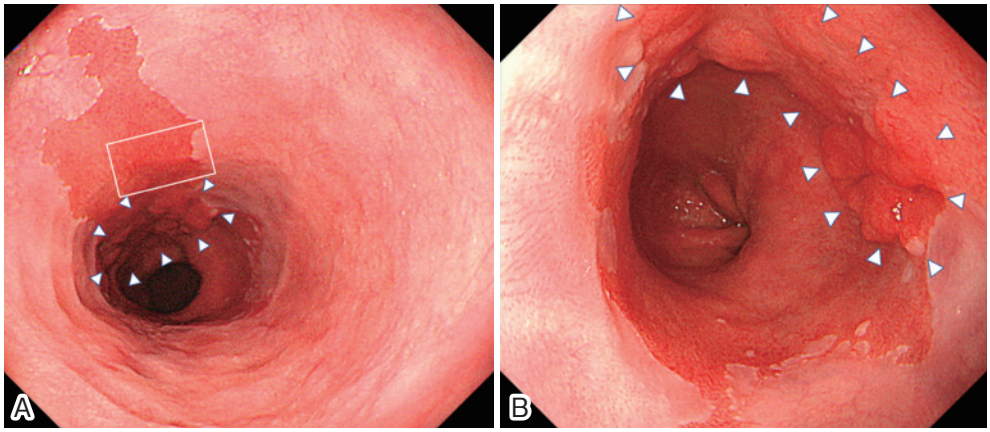

Figure 1 **A, B:** Conventional white light endoscopy shows long segment Barrett's esophagus (LSBE) extending from the esophagogastric junction to the anterior wall in a circumferential **(A)** and tongue-like appearance **(B)**. A 3.5-cm large protruding lesion with an erythematous tone was observed on the anterior-left wall of the LSBE (white arrowheads); however, white light endoscopy did not readily detect any other lesion **(A** and **B)**.

of *Helicobacter pylori* infection[3], the number of patients with Barrett's esophagus that is clearly associated with GERD has been gradually rising in Japan[4].

In Japan, the vast majority of patients with Barrett's esophagus (99%) have "short-segment Barrett's esophagus" (SSBE), while LSBE is extremely rare[5], moreover, EAC arising from LSBE is even more uncommon. Although esophagectomy is the standard treatment for advanced EAC, minimally invasive endoscopic radical R0 resection is preferred for superficial EAC (SEAC), especially in patients with early-stage cancer[6,7]. To achieve endoscopic radical R0 resection, however, it is necessary to accurately diagnose the extent of the tumor preoperatively[8].

The radical R0 resection rate for SEAC arising from LSBE is significantly lower than that of SEAC arising from SSBE (48% vs. 85%), and the preoperative determination of the extent of SEAC in patients with LSBE is particularly difficult[7,9].

Case Presentation

The patient was a 68-year-old man in good health with no remarkable medical history. Although he had no symptoms, he had been undergoing annual esophagogastroduodenoscopy under the direction of his previous physician as part of his annual full physical examination since 2015. While undergoing this procedure in April 2020, protruding lesions were discovered in lower esophagus, a biopsy revealed a histological diagnosis of well-differentiated tubular adenocarcinoma (group 5, tub1; the Japanese classification of gastric carcinoma). The patient was referred to our department for further examination and treatment in May 2020.

Barrett's esophagus extending from the esophagogastric junction to the anterior wall in a circumferential and tongue-like appearance, 4.5 cm in circumference and 6.5 cm in maximum extent (C4.5M6.5), was observed on conventional white light endoscopy. A 3.5-cm large protruding lesion with an erythematous tone was observed on the anterior-left wall of the LSBE, however, white light endoscopy did not readily detect any other lesion (Fig. 1A and 1B). On narrow-band imaging (NBI) magnification endoscopy (ME), the flat portion of the tongue-like Barrett's esophagus, which extended continuously to the oral side of the protruding lesion, was also found to exhibit a visible, pit-like irregular mucosal pattern of various sizes and shapes. It also appeared an irregular vascular pattern (Fig. 2, right side of the white dashed line) with irregularly bent and branching vessels of abruptly changed diameters, as well as an extensive flat type (type IIb) horizontal tumor extension. Four marginal biopsies (i.e., negative or mapping biopsies) of tissues that appeared non-dysplastic based on NBI-ME findings were all histologically negative. As no metastatic lesion was found on thoracoabdominal contrast-enhanced computed tomography, subtotal circumferential endoscopic submucosal dissection (ESD) was performed, excluding the non-dysplastic region (Fig. 3). We carried out the ESD

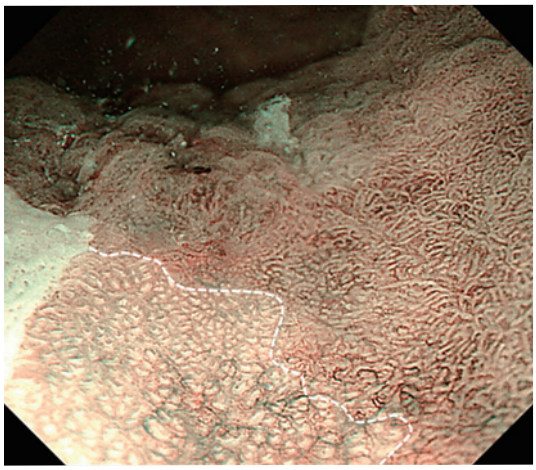

Figure 2 Narrow-band imaging magnification endoscopy shows irregular mucosal pattern and irregular vascular patterns (Fig. **2**, right side of the white dashed line) in the flat portion of the tongue-like Barrett's esophagus (white square in Fig. **1A**), which extended continuously to the oral side of the protruding lesion (white arrowheads in Fig. **1A** and **1B**).

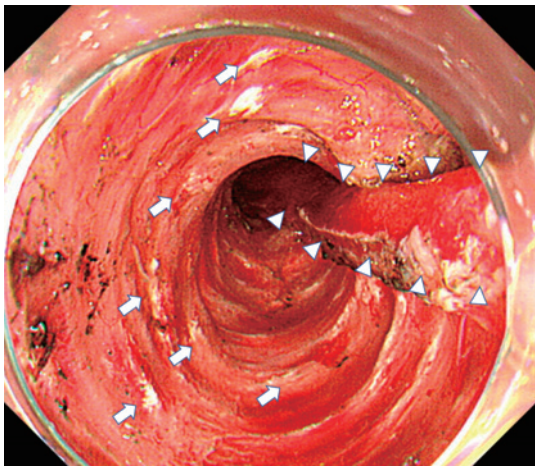

Figure 3 Conventional white light endoscopy shows remnant Barrett's mucosa (white arrowheads) and steroid injection points (white spots indicated by white arrows) immediately after subtotal circumferential endoscopic submucosal dissection.

with the patient under general anesthesia and the ESD procedure took 168 min. Histological analysis revealed a well-differentiated adenocarcinoma that was almost exactly coincident with the region diagnosed by preoperative NBI-ME. Extensive IIb extension was observed on the oral and anal (stomach) sides of the protruding tumor lesion, which was also consistent with the preoperative endoscopic diagnosis. The cancerous ducts had invaded into the deep mucosal muscular plate (pT1a-deep muscularis mucosa [DMM]). There were also three foci of carcinoma *in situ* smaller than 2 mm near the T1a-DMM cancer lesion. Both vascular invasion and dissection were negative, and en bloc radical resection (R0) was achieved.

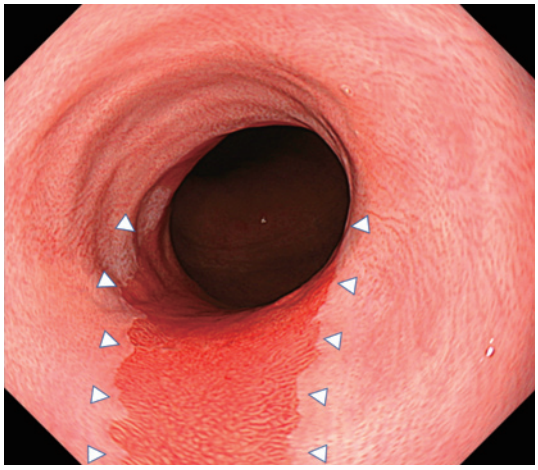

Figure 4 Conventional white light endoscopy shows remnant Barrett's mucosa in the 4 to 7 o'clock position (arrowheads). We found no stenosis and no evidence of cancerous remnants or recurrence in one year and 3 months after endoscopic submucosal dissection.

Given the extensive subtotal circumferential resection that was 6×5 cm in size, 100 mg of the steroid triamcinolone was injected into the residual submucosa of the ESD site immediately after the procedure as a prophylactic measure against stenosis. However, the patient developed postoperative stenosis 1 month after surgery, whereupon two endoscopic balloon dilation procedures were performed in succession 21 days apart, following which the stenosis eased and its symptoms disappeared. One year and 3 months after ESD, the patient had no signs of esophageal stenosis (Fig. 4), was able to consume regular food, and exhibited no evidence of cancerous remnants or recurrence. The patient provided informed consent for the publication of this report.

Discussion

The case we report herein is noteworthy for the following 3 reasons: 1) the occurrence of SEAC in an LSBE is extremely rare in Japan; 2) NBI-ME was able

to accurately diagnose the preoperative extent of SEAC in the LSBE, which is normally difficult to do, enabling R0 resection; and 3) refractory esophageal stenosis after extensive resection was avoided by steroid injection.

EAC is a common malignancy in Europe and the United States, however, it accounts for only 7.1% of all esophageal malignancies in Japan[10]. As mentioned above, the majority of EACs arise from Barrett's esophagus, and 99% of patients with this condition in Japan are classified as SSBE, while LSBE and SEAC are extremely rare.

A previous study of the outcomes of ESD in 524 superficial adenocarcinomas of the esophagus or high-grade dysplasia`s found that the R0 resection rate was 74.5%, moreover, 54 of the R1 resections (40.3%) had positive horizontal margins[9]. This highlighted the difficulty of determining the extent of lesions within LSBEs endoscopically. In patients with LSBE, low-grade dysplasia may spread widely proximal to the cancer or high-grade dysplasia, whereupon the extent of adenocarcinoma is very difficult to ascertain[7,9].

Although there is no direct evidence that ME with image enhancement, such as NBI, is useful in diagnosing the extent of SEAC, there are many reports of it being highly useful for its detection and characterization. And the sensitivities and specificities of this method are reportedly 90-100% and 92.9-100%, respectively[11-14]. Based on the idea that determining the extent of a tumor involves confirming the existence of a continuous cancerous lesion and delineating its margins, ME with image enhancement appears to enable the determination of the extent of superficial adenocarcinoma in patients with Barrett's esophagus. As such, its use is recommended for this purpose[8].

As discussed above, diagnosing tumor extent of cancerous lesions is particularly difficult in patients with LSBE[9]. In our patient, we closely observed the lesion using NBI-ME and performed perioperative biopsy to precisely determine its extent. As a result, R0 resection was achieved. The latest guideline[8] recommends NBI-ME and a biopsy of the tissue surrounding area of the lesion for determining the extent of the SEAC in patients with LSBE before performing endoscopic R0 resection. Histologically, the ESD specimen from our patient was determined to be well-differentiated adenocarcinoma with DMM invasion and negative vascular invasion. The cumulative rate of lymph node metastasis in previous studies of 305 patients with vascular invasion-negative differentiated adenocarcinoma and DMM involvement was extremely low at 0.3%[6,7,15,16], and most current guidelines do not recommend additional esophagectomy. Accordingly, we did not perform additional esophagectomy for our patient and followed him conservatively. The patient has had no recurrences to date and is in good condition after ESD.

SEACs occurring in conjunction with LSBE tend to be large lesions, and therefore require extensive endoscopic resection[17,18]. Because the esophagus is a small luminal organ, subtotal or more extensive circumferential resection may result in refractory postoperative stenosis. There have been numerous recent reports on the usefulness of oral steroid therapy and topical administration in preventing refractory esophageal stenosis after extensive ESD for squamous cell superficial carcinoma, and consensus has nearly been achieved on its use[8,19]. However, the usefulness of steroids in preventing stenosis following extensive resection for SEAC remains less clear.

Our patient underwent a 6 cm subtotal circumferential resection, which is a major ESD procedure. However, with steroid injection therapy, refractory esophageal stenosis was avoided with only 2 endoscopic balloon dilation procedures. The patient is currently able to consume a normal, pre-ESD diet. We therefore deduce that steroid therapy is effective in preventing refractory esophageal stenosis after extensive ESD for SEAC as well as for squamous cell carcinoma.

In a recent report from Japan, 2 of 6 patients with superficial adenocarcinoma accompanying LSBE who retained a portion of the Barrett's mucosa after ESD had metachronously developed multiple adenocarcinomas[20]. According to the systematic review in the latest guideline[8], the yearly incidence of metachronous cancer within the remaining Barrett's mucosa after endoscopic resection was 0.70% or 1.2% for LSBE. Although the yearly incidence of metachronous cancer after endoscopic resection for LSBE adenocarcinoma is lower than that for early gastric cancer (2.3%), it is much more difficult to observe the narrowing site with ESD scar and to detect early cancer in the remaining Barrett's esophagus than those in the stomach. Addition-

ally, in the ESD specimens, there were three foci of carcinoma *in situ* smaller than 2 mm near the T1a-DMM cancer lesion. Therefore, we plan to continue a strict long term follow-up regimen using NBI-ME every 6 months because of difficulties in endoscopic observation and detection as well as possibility of harboring minute cancer. Although there are currently no metachronous multiple cancers in the remnant Barrett's mucosa of our patient, we plan to continue a strict long term follow-up regimen using NBI-ME every 6 months.

In conclusion, we experienced a very rare case of SEAC occurring in LSBE and achieved curative R0 resection by subtotal circumferential ESD. Preoperative diagnosis of tumor extent using NBI-ME may be useful for characterizing the IIb extension of SEACs in LSBEs. Prophylactic therapy with local steroid injection can prevent refractory stenosis after quite extensive ESDs for SEACs.

Author contributions

K.G. wrote the manuscript. A.K., T.S., K.A., M.K., Y.I., T.Y., Y.A., T.T., M.K., K.N., T.M., A.Y., T.A., K.H., K.T., Y.M., and M.I. were engaged in clinical managements of this patient. K.I. established the histopathological diagnosis. A.I. supervised this case report.

Disclosure statement

The authors have no conflicts of interest to declare. The case study was not funded by any external sources of support.

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