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**Endoscopic Submucosal Dissection of a Minute Intramucosal Adenocarcinoma
in Barrett's Esophagus**

Running title: ESD for minute Barrett's cancer

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ABSTRACT

A 73-year-old man with short segmental Barrett's esophagus underwent esophagoscopy, and a slightly depressed, discolored lesion was found on the anterior wall of lower esophagus. Under a provisional diagnosis of differentiated adenocarcinoma without local lymph node metastasis, endoscopic submucosal dissection (ESD) was performed. En bloc resection with tumor-free lateral/basal margins was accomplished without complications. The resected area was 12X15 mm in size, whereas the neoplastic lesion was 4X4 mm. Histopathological examination confirmed intramucosal well-differentiated tubular adenocarcinoma without angiolymphatic invasion adjacent to the muscularis mucosae. Repeated esophagoscopy 6 months after ESD showed neither locally recurrent nor metachronous lesions. Considering that Barrett's esophagus is a precancerous condition, one may recommend eradication of both the neoplastic and non-neoplastic lesion with employing ESD.

Key words: endoscopic submucosal dissection, Barrett's adenocarcinoma, Barrett's esophagus

INTRODUCTION

Surgical treatment is still recommended in patients with Barrett's esophagus (BE) with high-grade intraepithelial neoplasia or early carcinoma limited to the mucosa. However, surgical mortality and postoperative morbidity, although decreasing, continue to be significant [1]. In recent years, the use of endoscopic techniques to deal with such incipient lesions in BE has increased [2]. Superficial BE cancers are not usually associated with locoregional lymph node involvement or distant metastasis [1,2]. Therefore, local treatment can provide a reasonable expectation of cure.

Endoscopic submucosal dissection (ESD) is an endoscopic resection method for superficial gastric cancers that was developed in Japan [3]. ESD involves circumferential cutting of the mucosa that surrounds the tumor, followed by dissection of the submucosa under the lesion. Using this method, almost any mucosal tumor, regardless of size and shape, can be resected en bloc. Recently, ESD has been used in other parts of the gastrointestinal tract, including the esophagus and colorectum [4, 5, 6]. However, its use in superficial BE cancers is still limited.

CASE REPORT

A 73-year-old man had upper gastrointestinal endoscopy for slight anemia (Hb 13 g/dL); all other laboratory test results were within normal limits. His physical

examination, as well as past and family histories, was non-contributory. On upper endoscopy, he was found to have a short segmental BE. Endoscopic recognition of BE was made by identification of the proximal margin of the gastric folds as the landmark. The palisade-shaped longitudinal vessels, which may be of value as esophageal landmark, were overlaid with the columnar-lined epithelia. Discolored flat mucosa on the anterior wall of the lower esophagus was identified within the columnar-lined epithelia (Figure 1A). The palisade-shaped longitudinal vessels, which may be of value as esophageal landmark, were overlaid with the columnar-lined epithelia of the other area. However, the palisade-shaped longitudinal vessels were invisible in the discolored area. On chromoendoscopy with indigo carmine (Figure 1B), a slightly depressed lesion was seen within the discolored area, and it was classified as a I Ib+I Ic type. Differentiated adenocarcinoma was suspected on the endoscopic biopsies. Endoscopic ultrasound and computed tomography excluded local lymph node metastasis. Thus, endoscopic submucosal dissection (ESD) was done (Figure 2). The lesion was lifted with submucosal injection of a glycerin and fructose solution. Then, a circumferential incision of the surrounding non-neoplastic mucosa was made using a Flex-knife (Olympus, Tokyo, Japan) with a high-frequency generator set at 80 W, while the Hook-knife (Olympus) was employed for ESD (output 60 W). En bloc resection with tumor-free lateral/basal margins was accomplished without complications. The

resected area was 12X15 mm, whereas the neoplastic lesion was 4X4 mm (Figure 3). An esophageal gland was found in the submucosa layer just under the cancer lesion resected (Figure 4). The histopathological examination confirmed the diagnosis of an intramucosal well-differentiated tubular adenocarcinoma adjacent to the muscularis mucosae without angiolymphatic invasion (Figure 5A). On immunostaining, the neoplasm was positive for p53 (Figure 5B). Repeat esophagoscopy 6 months after ESD showed neither recurrent nor metachronous lesions (Figure 6).

DISCUSSION

Endoscopic treatment, including endoscopic mucosal resection (EMR) and ESD, is an alternative to esophagectomy in BE patients with superficial neoplasms due to the low risk of lymph node involvement or distal metastases [1]. Endotherapy maximizes functional and organ preservation [2]. However, EMR has limitations with respect to the resectable tumor size; in many cases, piecemeal resection is unavoidable and has been occasionally linked to local recurrence [7]. ESD was first developed for en bloc removal of large gastric neoplasms. Recently, ESD has been used to remove esophageal squamous neoplasms or esophagogastric junction tumors including BE neoplasms with promising results [4,5]. It has been reported that the complete en bloc resection rate of ESD for esophagogastric junction tumors was no less than 97% (29/30) [5]. Perforation occurred in one case, but was safely managed

by rotatable clips. In our case, the intramucosal adenocarcinoma was successfully removed using ESD without any complications, such as perforation and bleeding. In line with our experience, Kakushima et al. described the complete removal of BE cancer lesions in 4 series [5]. Given these encouraging results, ESD should be more often considered as the primary treatment for superficial BE neoplasms. However, controlled studies comparing ESD and esophagectomy are needed.

We used several methods to minimize complications. First, a transparent hood was attached to the endoscope tip to ensure a good view during ESD. Second, to avoid perforation, a glycerin and fructose solution was injected to achieve higher and more sustained submucosal elevation. Finally, the operator was skilled in ESD and had considerable experience using ESD for relatively uncomplicated gastric tumors. Thus, ESD could be safely performed in patients with early BE cancer.

EMR is a treatment modality for early cancer of small size 1cm or less in diameter. For larger lesions, however, EMR is associated with risk of remnant disease or local recurrence [7]. Indeed the cancer lesion resected was 4x4mm in size, but the extent of the cancer lesion could not be exactly detected on endoscopic observation. We could not help but resect the affected lesion with sufficient lateral margin using ESD in order to prevent local recurrent disease. The whole resected area by ESD was 12x15mm in size, which included the cancer lesion with surrounding non-neoplastic columnar epithelia. Patients with a diagnosis of Barrett's esophagus are thought to be at risk of developing high-grade dysplasia or esophageal adenocarcinoma [1]. In Western countries, some endoscopists have

performed circumferential piecemeal EMR for not only mucosal Barrett's cancer but also surrounding non-neoplastic Barrett's mucosa in order to prevent local recurrence or the development of metachronous neoplastic lesions, albeit this concept is still controversial [8]. In principle, the ESD procedure may be used to eradicate the whole BE area, though this would be technically challenging. Further assessment of case series is necessary to evaluate the occurrence of complications, including post-ESD stenosis.

In Asia, including Japan, BE and its related neoplasm used to be less common than in Western countries [9]. However, in recent years, the number of reported cases of BE and its related neoplasm has increased in Japan [9]. Adenocarcinoma of the esophagus is still rare in Asia, although the annual death rate from adenocarcinoma of the esophagus has increased from 3.7 (1960) to 6.9 (1995) per 100,000 population [9]. Clearly, continued surveillance of changes in the epidemiology of BE and adenocarcinoma of the esophagus is needed. Furthermore, thorough observation of patients with risk factors for BE neoplasms using chromoendoscopy and/or magnifying endoscopy would contribute to the early detection of neoplasms, as seen in our case.

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Figure 1. A: On upper endoscopy, discolored flat mucosa on the anterior wall of the lower esophagus was identified within the columnar-lined Barrett's epithelia. The palisade-shaped longitudinal vessels were overlaid with the columnar-lined epithelia of the other area, whereas the palisade-shaped longitudinal vessels were invisible in the discolored area. B: On chromoendoscopy with indigo carmine, a slightly depressed lesion was seen within the discolored area, and it was classified as a IIb+IIc type.

Figure 2. Endoscopic submucosal dissection (ESD) was performed successfully.

Figure 3. The resected macroscopic specimen. A red line indicated the cancer lesion.

Figure 4. An esophageal gland was found in the submucosa layer just under the cancer lesion resected.

Figure 5. A: The histopathological examination shows a well-differentiated, intramucosal tubular adenocarcinoma adjacent to the muscularis mucosae without angiolymphatic invasion. B: On immunostaining, the neoplasm glands are positive for p53.

Figure 6. Repeat esophagoscopy 6 months after ESD showed neither recurrent nor metachronous lesions.