CASE REPORT
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A Submucosal Tumor-Like Recurrence of Early Esophageal Cancer after Endoscopic Submucosal Dissection

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Early esophageal cancer is defined as a tumor invading the mucosa with or without lymph node or distant organ metastasis. In the current guidelines for early esophageal cancer, absolute indication for endoscopic resection include lesions limited to the epithelium or lamina propria mucosa not exceeding two-thirds of the circumference, and relative indications include lesions limited to the muscularis mucosa or the upper third of the submucosal layer and not accompanied by clinical evidence of lymph node metastasis. After endoscopic submucosal dissection for early esophageal cancer, locally recurrent cancer can occur, especially in the case of incomplete resection. Here, we report a rare case of a submucosal tumor-like recurrence after endoscopic resection of early esophageal cancer.

Key Words: Esophageal neoplasms; Endosonography; Endoscopic resection; Recurrence

INTRODUCTION

Early esophageal cancer (EEC) is defined as a tumor limited to the mucosa with or without lymph node (LN) or distant organ metastasis.[1] When the tumor is limited to the mucosa of the esophagus, endoscopic resection (ER) is recommended as an alternative therapeutic modality because it is associated with a long-term survival outcome, similar to that achieved by surgery.[2,3] Nevertheless, there are some limitations to the efficacy and safety of ER; this technique is associated with post-ER recurrence, especially when a lesion of >20 mm is removed by piecemeal resection.[4] To overcome these limitations, endoscopic submucosal dissection (ESD) was introduced. ESD enables en bloc resection regardless of the size or presence of submucosal fibrosis.[5]

To date, there has been scant long-term follow-up data on ESD for EEC. Several studies have reported local recurrences after ESD for EEC, but few patients with complete resection during ESD have recurrent cancer.[5-9] Incomplete resection can leave residual disease and thus some possibility of local recurrence. Here, we report a submucosal tumor (SMT)-like local recurrence after ESD for EEC.

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CASE REPORT

A 68-year-old man presented with dysphagia of 1-month duration. Three years previously, he had been diagnosed with EEC of the lower esophagus judged to be T1aN0M0 (stage I) and had undergone ESD (Fig. 1A, B). Upon pathological examination, a 1.4×1.1 cm well-to-moderately differentiated squamous cell carcinoma (SCC) was found to have invaded the muscularis mucosa (MM) without penetration (Fig. 1C). The vertical resection margin was negative for carcinoma, but the distal resection margin was positive for SCC and this ESD was regarded as an incomplete resection. However, on follow-up endoscopy (at 4th day after ESD), the endoscopic findings suggesting remnant cancer was not seen and argon plasma coagulation (APC) was performed for the distal margin. Thereafter, we checked the existence of residual carcinoma by serial follow-up studies, including chest computed tomography (CT) scans and endoscopy with biopsy over the course of 18 months (Fig. 1D). We identified no recurrence on the esoph-

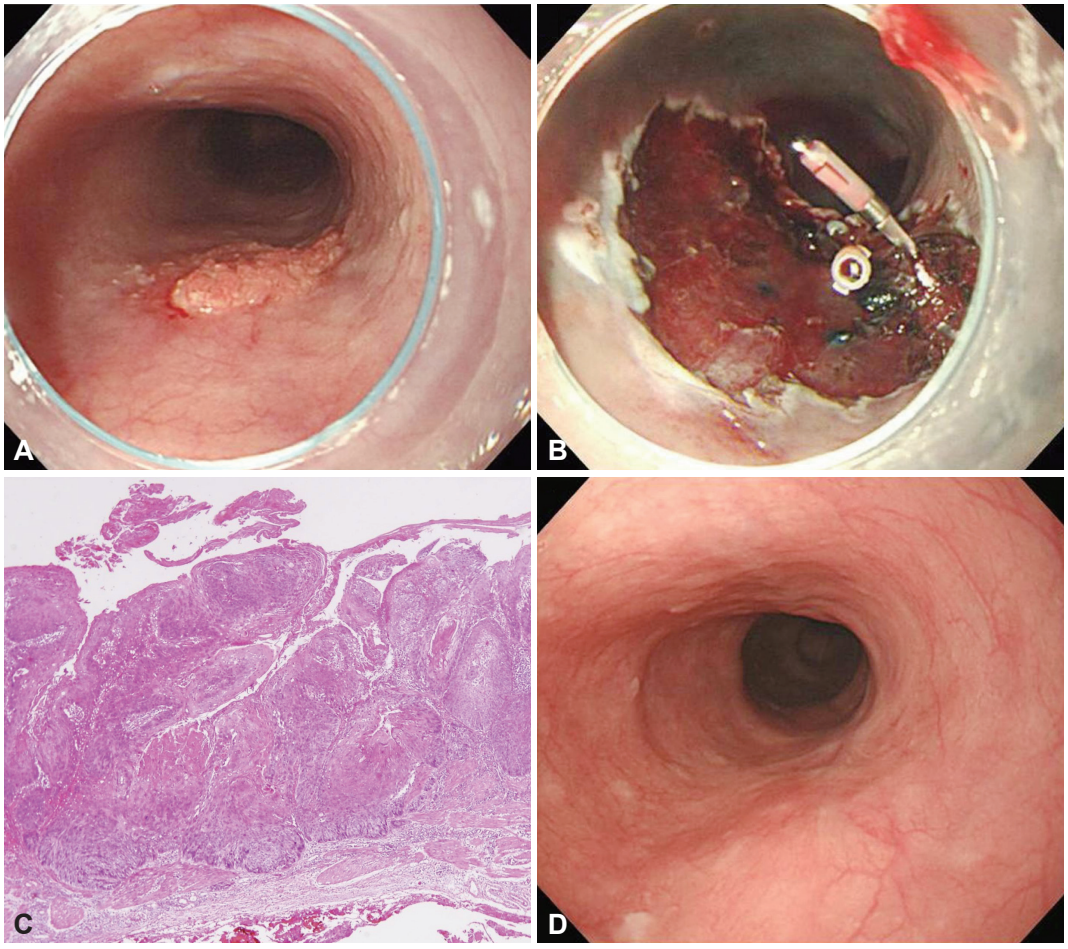

Fig. 1. Endoscopic and histologic findings at the time of endoscopic submucosal dissection (ESD) and follow-up. (A) A 1.5-cm superficial elevated lesion was observed in the lower esophagus (33 cm from the incisor teeth). (B) This lesion was resected by ESD. (C) Histologic findings revealed that the lesion had invaded the muscularis mucosa (H&E stain, ×200). Because the distal margin of the resected specimen was positive for carcinoma, additional argon plasma coagulation was employed. (D) On follow-up endoscopy (18 months after ESD), no recurrence was observed.

agus. The patient was then lost to follow-up.

On the current visit, the patient reported that he was a current smoker with a 20 pack-year smoking history. Laboratory findings were unremarkable. On the endoscopic images, the post-ESD scar was observed at the lower esophagus, but it looked like an SMT (Fig. 2A). At its center, a tiny nodular change was seen, and this was unstained by lugol chromoendoscopy (Fig. 2B). On magnified endoscopy with narrow band imaging, an irregular microvascular pattern was observed in the nodular area (Fig. 2C). Endoscopic biopsy revealed recurrent SCC. On endoscopic ultrasonography (EUS), the cancer was found to have invaded the muscularis propria, but there was no LN enlargement (Fig. 2D). Chest CT scans showed a 1.5 cm low density mass at the lower esophagus, and positron emission tomography showed increased ^{18}fluoro-2-deoxyglucose uptake in the same area. Ivor-Lewis esophagectomy with 2-field LN dissection was performed. On gross examination, the esophagus was found to have a relatively ill-defined white solid mass, 1.5×1.5 cm in size, located mainly on the submucosa and muscularis propria in cross section (Fig. 2E). On pathological examination, the SCC was found to have invaded the adventitia with a mixed infiltrative and expanding growth pattern (Fig. 2F). There was no evidence of LN metastasis. The patient subsequently underwent six cycles of adjuvant chemotherapy (5-fluorouracil plus cisplatin). He is currently alive, and there has been no recurrence throughout the 17-month follow-up period.

DISCUSSION

In 1966, Takubo et al.[10] coined the term 'EEC,' but they did not provide a definition of it. In the first edition of the guidelines issued by the Japan Esophageal Society (JES), EEC was defined as mucosal or submucosal carcinoma of the esophagus regardless of LN metastasis. Recently, in the 10th edition of the guidelines issued by the JES, EEC was defined as a lesion

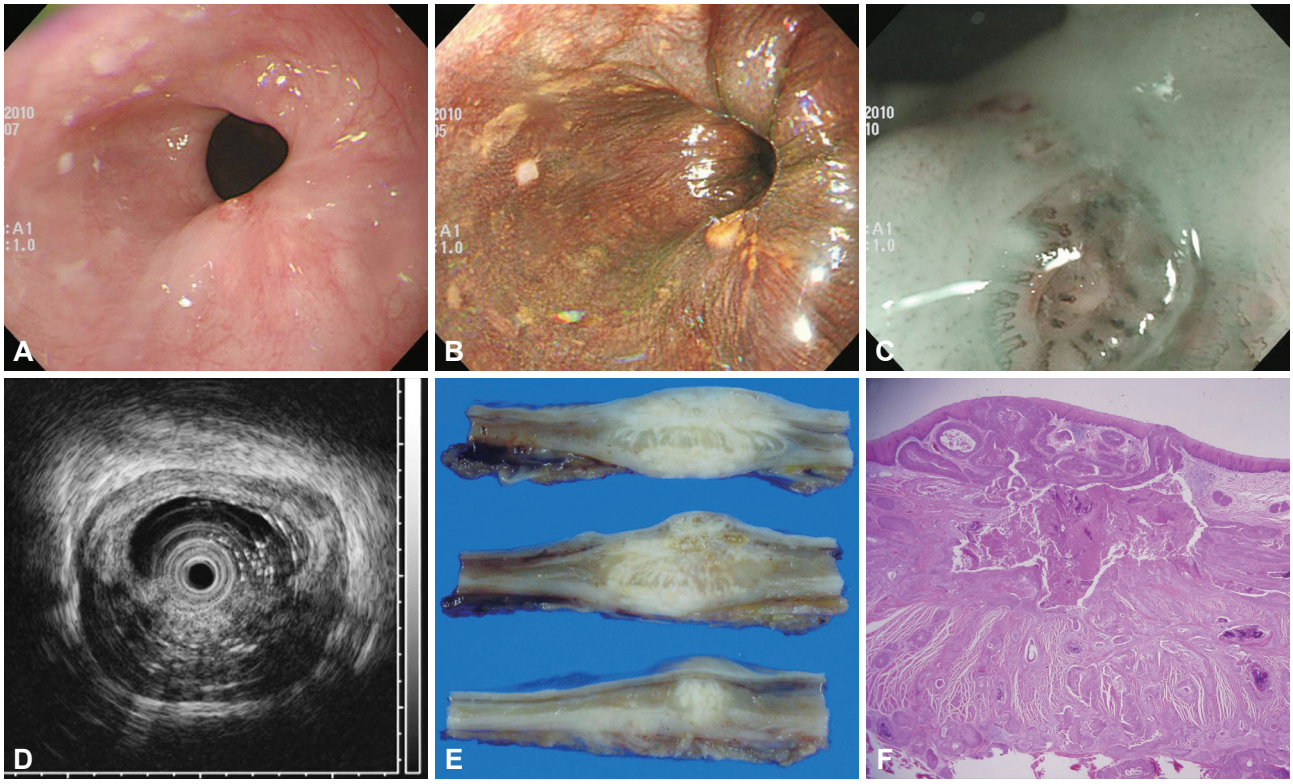

Fig. 2. Endoscopic, endoscopic ultrasonography (EUS), and histologic findings at the time of recurrence. (A) A submucosal tumor-like lesion with central nodular change was seen at the previously resected area. (B) After lugol spraying, only the central nodular area was unstained. (C) Magnified endoscopy with narrow band imaging showed an abnormal microvascular pattern in the central nodular area. (D) EUS revealed that the tumor had invaded the muscularis propria. (E) Gross findings after esophagectomy included a relatively ill-defined white solid mass in the submucosa and muscularis propria measuring 1.5×1.5 cm. (F) Histological examination showed that the lesion had invaded the adventitia and had a mixed infiltrative and expanding growth pattern (H&E stain, ×200).

limited to the MM, regardless of LN or distant organ metastasis (e.g., EEC: T1aNxMx).[1] A lesion that has invaded the mucosal and submucosal layers is designated a superficial esophageal cancer, regardless of LN or distant organ metastasis.[1] In the case reported here, a patient initially diagnosed with EEC had a carcinoma that invaded the MM after ESD.

To date, the indications for ESD have been based on the presence of LN metastasis.[11] The factors associated with LN metastasis are invasion depth, venous invasion, lymphatic infiltration, and tumor grade and histology.[10-12] According to the 2007 guidelines issued by the JES, absolute indications for ER are lesions limited to the mucosal epithelium (EP) or lamina propria mucosa (LPM) and not exceeding two-thirds of the circumference because these lesions have little possibility of LN metastasis. Lesions that have extended into the MM, those with minute submucosal invasion (SM1) not accompanied by clinical evidence of LN metastasis, or EP or LPM lesions exceeding two-thirds of the circumference are relative indications for ER because of the possibility of LN metastasis and postoperative complications.[11] Fujishiro and Kodashima[13] recommended that EP or LPM lesions exceeding 15 mm and MM or SM1 lesions not accompanied by clinical evidence of LN metastasis are good indications for ESD. In addition, lesions with submucosal fibrosis, such as residual or recurrent lesions occurring after ER or chemoradiotherapy, and with low possibility of LN metastasis are considered as extended indications for ESD. On the basis of these data, we performed ESD and additional APC for our patient and found no recurrence on endoscopy and chest CT examinations performed during an 18-month follow-up.

Several studies have reported that patients with complete resection during ESD have a very low risk of local recurrence, but there remains a possibility of local recurrence, particularly in the case of incomplete resection during ESD.[5-9] Ono et al.[5] reported one case of local recurrence among patients with incomplete resection and no local recurrence among patients with complete resection during a mean follow-up of 632 days of patients who underwent ESD for 107 superficial esophageal squamous cell neoplasms. Yoshinaga et al.[6] reported that patients with completely resected superficial adenocarcinoma at the esophageal junction during ESD had no recurrence or metastasis during a median follow-up period of 30.1 months. However, in one patient with incomplete resection, lung metastases were found 3 years after the ESD.[6] In another stu-

dy of 58 consecutive esophageal squamous cell neoplasms resected by ESD, one incompletely resected lesion recurred locally 6 months after the ESD and was treated successfully by a second ESD procedure.[7] As indicated in these reports, more favorable outcome was produced with complete resection than with incomplete resection for EEC.

In our patient, EEC was initially removed with an incomplete ESD resection followed by APC; but after 3 years, we performed a second operation for a locally recurrent SMT-like carcinoma. To the best of our knowledge, this is the first case report of a recurrent SMT-like cancer occurring after ESD for EEC. The possible mechanism underlying how locally recurrent SMT-like cancer occurred after incomplete ESD was suggested as follows: after incomplete ESD, the remnant cancer might have been buried under the normal surrounding squamous EP during the healing process. This buried cancer might grow slowly within the deep layer of the esophageal wall without exposure to the surface. This course would lead to a SMT-like recurrence, which is difficult to diagnose. A few studies have reported buried Barrett's EP associated with malignant transformation after ablation therapy for Barrett's esophagus.[14,15]

There are few reports on the APC after incomplete ESD of EEC. However, APC has been used effectively in the Barrett's dysplasia[16,17] and early gastric cancer.[18] Therefore, even though other treatment options such as surgery or concurrent chemoradiotherapy could be considered in the case of incomplete resection, we chose APC to the distal margin and close follow-up in this case.

In summary, we reported a very rare SMT-like recurrent carcinoma occurring after incomplete ESD for EEC. This suggests that local recurrence could occur as uncommon forms, such as SMT, after ER for EEC.

Conflicts of Interest

The authors have no financial conflicts of interest.

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