A case of simultaneous superficial hypopharyngeal and superficial esophageal cancers treated by endoscopic resection

Running title: Simultaneous ELPS and ESD

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Abstract

In recent times, the diagnosis and treatment of superficial laryngopharyngeal cancers has been receiving a lot of attention. Here, we present a case of superficial hypopharyngeal cancer and superficial esophageal cancer for which endoscopic laryngo-pharyngeal surgery (ELPS) and endoscopic submucosal dissection (ESD) were performed simultaneously. The patient was a 67-year-old male. During his follow-up for distal gastrectomy performed earlier for stomach cancer, an upper gastrointestinal endoscopy revealed three primary cancers: superficial hypopharyngeal cancer, superficial esophageal cancer, and esophagogastric junction cancer. Total resection of the remnant stomach was performed followed by hypopharyngeal ELPS combined with esophageal ESD. He developed aspiration pneumonia after the surgery; however, he recovered and was discharged on the 16th day. Thus, safe and effective endoscopic therapy can be performed even for double superficial cancers of the laryngopharynx and esophagus.

Keywords: ELPS, ESD, double cancer, esophageal cancer, pharyngeal cancer
Introduction

In recent times, there has been a rise in the incidence of superficial cancers in the pharyngeal area, and accordingly, a lot of attention is being paid to the diagnosis and treatment of superficial pharyngeal cancers. In this paper, we are presenting a case of superficial hypopharyngeal cancer and superficial esophageal cancer for which simultaneous endoscopic laryngo-pharyngeal surgery (ELPS) and endoscopic submucosal dissection (ESD) were performed. Moreover, we especially mention the efficacy after considering quality of life (QOL) including relative indication, and the safety mostly postoperative management.

Case

The patient was a 67-year-old male that had been visiting our department for four years as an outpatient after undergoing distal gastrectomy (Roux-en-Y anastomosis reconstruction) for stomach cancer. He has been smoking 40 cigarettes/day for 44 years and drinking three cups of shochu (Japanese distilled spirits) every day.

His post-operative, follow-up blood tests for stomach cancer revealed elevated levels of carcinoembryonic antigen (CEA) at 13.2 ng/mL. An upper gastrointestinal endoscopy was performed, and he was diagnosed with three primary cancers: superficial hypopharyngeal cancer, superficial esophageal cancer, and esophagogastric junction cancer.
Physical findings were: height 161 cm, weight 42.8 kg, and a surgical scar in the exact middle of the upper abdomen, with no palpable masses in the abdomen.

Upper endoscopy findings included a well-circumscribed ulcerative lesion (Type 2) found at the squamocolumnar (SC) junction at the 7 o'clock position (esophagogastric [EG] region, Siewert type II). The biopsy confirmed it to be positive for mucinous adenocarcinoma (Fig. 1a). Mucosal lesions with irregular margins accompanied by white lichen on some parts (Ce, Type 0-IIc) were noted on the right side of the esophageal wall, 18 cm from the incision line. A biopsy confirmed it as squamous cell carcinoma (SCC) (Fig. 1b). Furthermore, a protruded lesion (Type 0-IIa) measuring 10 mm was found in the left piriform sinus, which was confirmed to be SCC in the biopsy (Fig. 1c). Endoscopic diagnostics were cT1a for esophageal and pharyngeal cancers, and cT2 for esophagogastric junction cancer, respectively.

CT scanning revealed that no neoplasm was noted in the esophagogastric junction, cervical esophagus, or hypopharynx, and there were no findings indicating lymph node metastasis or distant metastasis.

Based on the above findings, a treatment plan was considered. Due to request of the patient who didn’t want to receive highly invasive therapy such as chemoradiation therapy, we planned to resect esophagogastric junction cancer by surgery first, and then perform simultaneous ELPS and ESD for superficial hypopharyngeal cancer and esophageal cancer.

A total resection of the remnant stomach was performed as treatment for esophagogastric junction
cancer at first. The post-operative pathological diagnosis was esophagogastric junction cancer UAe (Siewert type II), Less, Type 2, 24 x 25 mm, muc>>por 1, pT1b (SM), N0 (0/6), M0, pStage IA.

The post-operative course was satisfactory, and he was discharged from the hospital on the 11th day.

He was scheduled for simultaneous hypopharyngeal ELPS and esophageal ESD two months after the total resection of the remnant stomach.

The blood biochemistry tests on admission for the ELPS and ESD showed anemia (Hb 9.4 g/dl and Ht 28.8%). Mild liver dysfunction was also noted (AST 43 U/L and γ-GTP 94 U/L). The tumor marker levels were: CEA 5.0 ng/mL, CA19-9 13.2 U/mL, SCC 1.7 mg/mL, and CYFRA 6.4 ng/mL.

ELPS for the hypopharyngeal cancer and ESD for the esophageal cancer were performed under general anesthesia (Fig. 2). Surgical time was 84 minutes.

The intraoperative findings revealed Lugol 1/3 circumference unstained lesions of Type 0-IIc in the cervical esophagus and Lugol unstained lesions of Type 0-IIa in the left piriform sinus in the hypopharynx region. After the marking of the exterior margins of the tumor, an epinephrine-saline solution was injected into the submucosal space, and the submucosa was separated and resected en bloc (Fig. 3). There were no intra-operative complications. Extubation was performed immediately after the surgery, and the patient was returned to the general ward because his respiratory status was stable.

The post-operative pathological diagnosis confirmed the hypopharyngeal cancer as SCC, Type0-IIa,
22 x 23mm, pT1a (LPM), ly(-), v(-), pHM0, pVM0, pR0, with the cervical esophageal cancer as SCC, Type0-IIc, 16 x 10mm, pT1b (SM1), ly(-), v(-), pHM1, pVM0, pR1 (Fig. 4).

On the second post-operative day, he developed a fever and increased sputum volume, which was diagnosed as co-existing aspiration pneumonia, for which sulbactam sodium/ampicillin sodium were administered and intraoral drainage was performed. Water intake was started on the fourth day; meals were restarted on the eighth day. On the 16th day, he had recovered and was discharged. Additional surgical resection or chemoradiation of the cervical esophageal cancer was considered, but the patient, whose physical energy was limited due to the total gastrectomy, opted not to receive highly invasive treatment, and chose to receive a chemotherapy alone. He was started on chemotherapy with 5-Fluorouracil and Cisplatin in combination (FP therapy) two months after the surgery. The FP therapy, however, was discontinued after two courses as per the request of the patient, whose vitamin B12 deficiency anemia was worsening because of nutrient malabsorption due to the gastric resection and prior excessive alcohol intake. It has been 1.2 years since the ELPS/ESD, and the patient has experienced no relapse.

Discussion

Hypopharyngeal cancers are commonly detected in advanced stages after the onset of subjective symptoms such as throat pain and have a poor five-year survival rate of 30–40%.1-3 In case of
advanced hypopharyngeal cancers, surgery and radiation therapy can greatly impair the QOL.

Thanks to the recent advancement of NBI magnifying endoscopy, pharyngeal and esophageal cancers have become more frequently detected when they are still superficial. For patients with superficial cancer, a less invasive and less QOL-impairing treatment option, if available and appropriate, should be pursued.

ELPS, a procedure in which forceps and an electrical scalpel are inserted through the mouth to perform endoscopy-assisted submucosal separation, was conceptualized and developed by Omori et al. in 2004 as a technique to treat superficial pharyngeal cancer. After intratracheal intubation under general anesthesia, the patient’s cervical region is extended by clamping the intubation tube in the median position with the face positioned upward to insert a curved laryngoscope and thereby secure a wide view of the pharynx. The practitioner and operator stand at the head side of the patient and first mark 1–2 mm outside the boundary of the lesion using an electrical scalpel. Next, a local injection of an epinephrine-saline solution is administered, and a circumferential incision is made 1–2 mm outside the marking. Furthermore, countertraction is applied using forceps to separate the submucosa, and the lesion is resected en bloc.

Procedural complications of ELPS include hemorrhage, post-operative laryngeal edema, stenosis and dysphagia, vocal cord injury, post-operative transient vocal cord paralysis, and subcutaneous emphysema, mediastinal emphysema, mediastinitis, and mediastinal abscess due to perforation,
among others. The respiratory status of this particular patient was stable even immediately after extubation, with neither airway constriction nor hoarseness observed. We hence determined that his condition was manageable at the general ward. On post-operative Day 2, however, he was diagnosed with aspiration pneumonia when saliva accumulation was noted in the mouth. His aspiration pneumonia was alleviated after antibiotic administration and intraoral drainage. His oral intake resumed after the aspiration pneumonia remitted. He did not have dysphagia or aspiration, nor did he have a relapse of the aspiration pneumonia, which all suggested that no post-operative cicatricial stenosis of the hypopharynx had preceded the aspiration pneumonia. We concluded, therefore, that the aspiration pneumonia was attributable to impaired saliva swallowing associated with transient post-operative edema of the region from the hypopharynx to the cervical esophagus.

Kishimoto et al. have reported the safety, outcome and feasibility of ELPS in elderly patients aged 75 or older. In 19 cases, although 4 cases had positive margin, no local recurrence occurred in those cases. Postoperative aspiration pneumonia occurred in 2 cases who were suspected to invade the muscle layer, and these complications were safely managed. These results suggested that the endoscopic resection might be acceptable for patient who was vulnerable from the point of view of oncological outcomes and safety.

Pharyngeal cancer and esophageal cancer often occur as multiple or double cancers that develop in a
metachronous manner, and their risk factors are believed to include high alcohol consumption, a long history of cigarette smoking, and partial ALDH2 deficiency. Successful cases of simultaneous endoscopic resection of superficial pharyngeal and esophageal cancers have been reported, but the number is still few, and the safety or effectiveness of the procedure has been not discussed enough.

In this case mentioned herein, we succeeded in simultaneously yet safely resecting superficial hypopharyngeal cancer and superficial esophageal cancer by using the ELPS and ESD procedures. Pathological diagnosis was pT1b(SM1), pHM1 in esophageal specimen. However, the tumor cells infiltrated in submucosal layer at only one point and no vessel invasion was found. Despite recommendation of additional treatment for patient with pT1b after endoscopic resection by Guideline for Diagnosis and Treatment of carcinoma of the Esophagus 2017, the patient hoped to avoid highly invasive therapy such as surgery or chemoradiation therapy. Although the patient has had no relapse until now, close surveillance should be required.

When treating a patient that has high risk factors of pharyngeal or esophageal cancer, it is particularly important to check the presence of a double cancer before choosing a treatment approach and equally important to keep paying close attention, in post-treatment follow-ups, to the metachronous occurrence of double or multiple cancers. It is anatomically difficult to observe the area from the pharynx to the cervical esophagus with the current endoscopy methods; as a solution, the “trumpet maneuver”
proposed by Kawada et al., a method for observing the pharynx, may work. The trumpet maneuver allows fora wide view of the pharynx by inserting an endoscope via the nose and making the patient exhale strongly in such a way as to inflate the cheeks while the mouth is closed. If we become able to spot double cancers at an earlier stage than we do today by introducing the trumpet maneuver or another method that enables us to perform a more thorough observation of the hypopharynx and esophagus during an upper endoscopy, we believe that the endoscopic and simultaneous resection of such double cancers will be a feasible option that also helps patients maintain their QOL.

Conclusion

We performed ELPS and ESD on a patient with double superficial cancers of the hypopharynx and esophagus. We successfully managed postoperative complication and maintained QOL after treatment by ELPS combined with esophageal ESD.

Conflict of Interest

The authors declare no conflicts of interest associated with this manuscript.

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Figure legends

Fig. 1:

a. Well-circumscribed ulcerative lesion (Type 2) at the SC junction at the 7 o'clock position (arrow heads)

b. Superficial 1/3 circumference ulcerative lesions (Type 0-IIc) associated with white lichen on the right side of the cervical esophageal wall, 18 cm from the incision line (arrow heads)

c. Whitish protruded lesion (Type 0-IIa) in the left piriform sinus (arrow heads)

Fig. 2:

a. Curved laryngoscope

b. The mouth is opened using an oral wider (arrow) with a tracheal intubation tube secured medially.

c. A curved laryngoscope (arrow) is inserted and fixated, securing a wide view of the larynx.

Fig. 3:

a-b. Esophageal endoscopic submucosal dissection
c-d. Hypopharyngeal endoscopic laryngopharyngeal surgery

Lugol is sprayed to determine the extent of the disease, and the entire circumference of the lesion is marked about 1–2 mm outside its borders. A local injection of an epinephrine-saline solution is administered, a circumferential incision is made 1–2 mm outside the marking, and enbloc resection of submucosa is performed.

Fig. 4:

a. Pathological examination revealed that the tumor cells were limited within mucosal lamina propria in hypopharyngeal specimen (pT1a). (x 400)

b. In esophageal specimen, the tumor cells infiltrated in submucosal layer at only one point (pT1b). (x 100)

c. There were tumor cells at the adjacent point of burned edge of esophageal specimen. (pHM1). (x 400)
Figure 1

(a) Image a

(b) Image b

(c) Image c
Figure 2
Figure 3
Figure 4