—Case Reports—

Simultaneous Endoscopic Resection of Superficial Cancers of the Hypopharynx and Esophagus: A Case Report

Miki Miyazawa, Takeshi Shimakawa, Shinichi Asaka, Kentaro Yamaguchi, Minoru Murayama, Takebumi Usui, Hajime Yokomizo, Shunichi Shiozawa, Takao Katsube and Yoshihiko Naritaka

Department of Surgery, Tokyo Women's Medical University Medical Center East, Tokyo, Japan

Diagnosis and treatment of superficial laryngopharyngeal cancers has recently received considerable attention. Here, we present a case of superficial hypopharyngeal cancer and superficial esophageal cancer treated with simultaneous endoscopic laryngopharyngeal surgery (ELPS) and endoscopic submucosal dissection (ESD). The patient was a 67-year-old man. During his follow-up for distal gastrectomy—performed earlier for stomach cancer—upper gastrointestinal endoscopy revealed three primary cancers: a superficial hypopharyngeal cancer, superficial esophageal cancer, and esophagogastric junction cancer. After total resection of the remnant stomach, combined hypopharyngeal ELPS with esophageal ESD was performed. He developed aspiration pneumonia after surgery but 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. (J Nippon Med Sch 2020; 87: 294–298)

Key words: ELPS, ESD, double cancer, esophageal cancer, pharyngeal cancer

Introduction

The incidence of superficial pharyngeal cancers is increasing, and much attention has thus been focused on diagnosis and treatment of such cancers. We present a case of superficial hypopharyngeal and esophageal cancers that were treated by simultaneous endoscopic laryngopharyngeal surgery (ELPS) and endoscopic submucosal dissection (ESD). We analyze the effectiveness of treatment and the effect on quality of life (QOL), as well as surgical indications and safety (particularly postoperative management).

Case

The patient was a 67-year-old man who had been visiting our department for 4 years as an outpatient after undergoing distal gastrectomy (Roux-en-Y anastomosis reconstruction) for stomach cancer. He reported smoking 40 cigarettes/day for 44 years and drinking 3 cups of *shochu* (Japanese distilled spirits) daily.

During a follow-up examination, blood testing for stomach cancer revealed an elevated carcinoembryonic antigen (CEA) level: 13.2 ng/mL. Upper gastrointestinal endoscopy showed 3 primary cancers: a superficial hypopharyngeal cancer, superficial esophageal cancer, and esophagogastric junction cancer. His physical findings were height 161 cm and weight 42.8 kg. He had a surgical scar exactly in the middle of the upper abdomen and no palpable masses in the abdomen.

Upper endoscopy showed a well-circumscribed ulcerative lesion (Type 2) at the squamocolumnar (SC) junction at a 7 o'clock position (esophagogastric [EG] region, Siewert type II). Analysis of a biopsy specimen confirmed positivity for mucinous adenocarcinoma (**Fig. 1a**). Mucosal lesions with irregular margins and 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. Analysis of the biopsy specimen showed squamous cell carcinoma (SCC) (**Fig. 1b**). Furthermore, a protruding lesion (Type 0-IIa) measuring 10 mm was present in the left piriform sinus, and was confirmed to be SCC after

Correspondence to Miki Miyazawa, Department of Surgery, Tokyo Women's Medical University Medical Center East, 2–1–10 Nishiogu, Arakawa-ku, Tokyo 116–8567, Japan
E-mail: miyazawa.miki@twmu.ac.jp
https://doi.org/10.1272/jnms.JNMS.2020_87-509
Journal Website (https://www.nms.ac.jp/sh/jnms/)

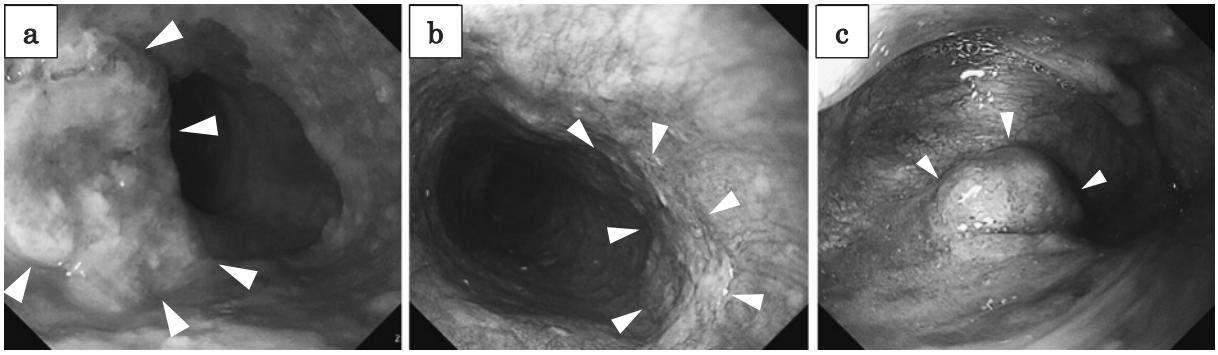

Fig. 1
a. Well-circumscribed ulcerative lesion (Type 2) at the SC junction at a 7 o'clock position (arrowheads)
b. Superficial 1/3 circumference ulcerative lesions (Type 0-IIc), with white lichen, on the right side of the cervical esophageal wall, 18 cm from the incision line (arrowheads)
c. Whitish protruding lesion (Type 0-IIa) in the left piriform sinus (arrowheads)

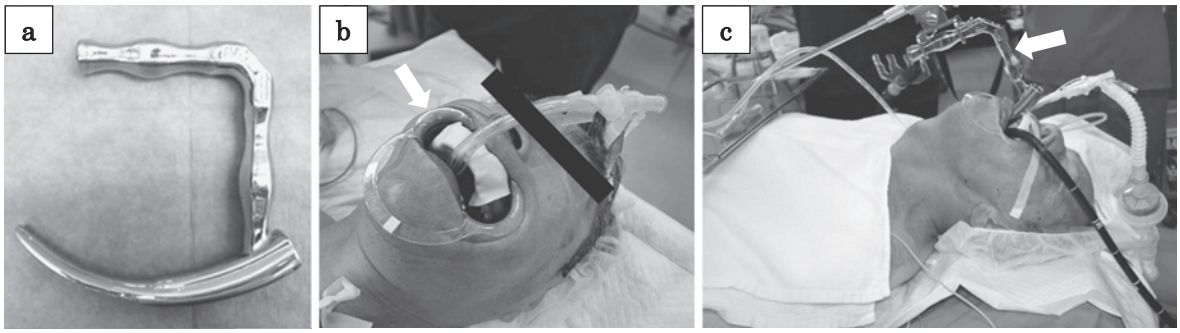

Fig. 2
a. Curved laryngoscope
b. The mouth is opened with an oral wider (arrow); the tracheal intubation tube is secured medially.
c. A curved laryngoscope (arrow) is inserted and fixated and provides a wide view of the larynx.

the biopsy (**Fig. 1c**). The endoscopic diagnoses were cT1a for the esophageal and pharyngeal cancers and cT2 for the esophagogastric junction cancer.

CT scans showed no neoplasm in the esophagogastric junction, cervical esophagus, or hypopharynx and no evidence of lymph node metastasis or distant metastasis. On the basis of these findings, a treatment plan was developed. Because the patient declined highly invasive therapy, such as chemoradiation therapy, we chose to resect the esophagogastric junction cancer and then perform simultaneous ELPS and ESD for treatment of the superficial hypopharyngeal and esophageal cancers.

First, total resection of the remnant stomach was performed as treatment for the esophagogastric junction cancer. The postoperative pathological diagnosis was esophagogastric junction cancer UAe (Siewert type II), Less, Type 2, 24 × 25 mm, muc>>por 1, pT1b (SM), N0 (0/6), M0, pStage IA. The postoperative course was satisfactory, and he was discharged from hospital on the 11th day. He was scheduled for simultaneous hypopharyngeal ELPS and esophageal ESD 2 months after the total resection of the remnant stomach. Blood biochemistry tests on admission for ELPS and ESD showed anemia (Hb 9.4 g/dL, Ht 28.8%) and mild liver dysfunction (AST 43 U/L, γ-GTP 94 U/L). 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 hypopharyngeal cancer and ESD for esophageal cancer were performed under general anesthesia (**Fig. 2**). The surgical time was 84 minutes.

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

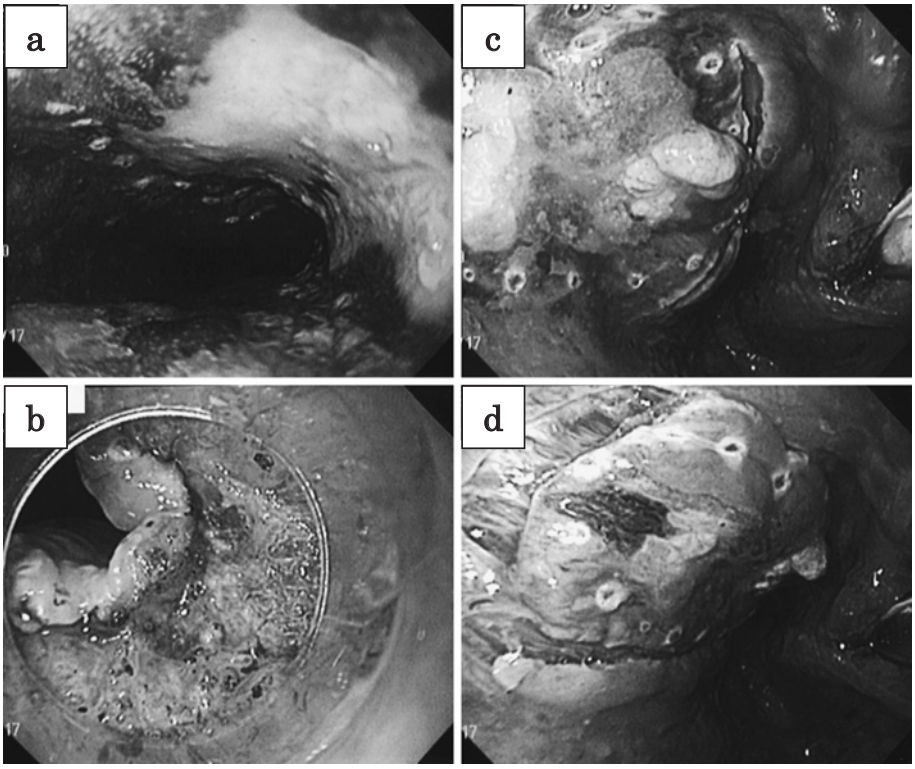

Fig. 3
a-b. Esophageal endoscopic submucosal dissection
c-d. Hypopharyngeal endoscopic laryngopharyngeal surgery
Lugol is sprayed to determine the extent of the disease, and the entire circumference of the lesion is marked to about 1-2 mm outside its borders. An epinephrine-saline solution is injected locally, a circumferential incision is made 1-2 mm outside the marking, and the submucosa is resected en bloc.

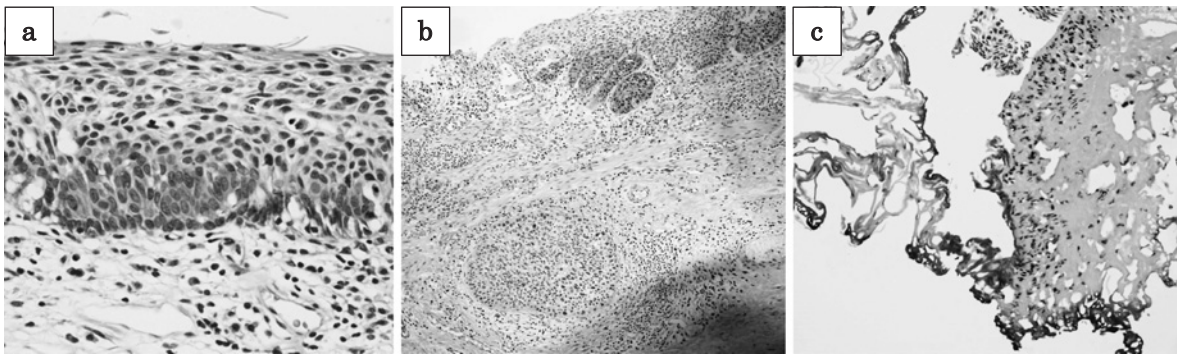

Fig. 4
a. Pathological examination of a hypopharyngeal specimen showed a few tumor cells within the mucosal lamina propria (pT1a) (×400).
b. In an esophageal specimen, tumor cells infiltrated the submucosal layer at only one point (pT1b) (×100).
c. Tumor cells were adjacent to the burned edge of an esophageal specimen (pHM1) (×400).

ratory status was stable. Postoperative pathological diagnosis of the hypopharyngeal cancer indicated SCC—Type 0-IIa, 22 × 23 mm, pT1a (LPM), ly(-), v(-), pHM0, pVM0, pR0. The cervical esophageal cancer was also SCC—Type 0-IIc, 16 × 10 mm, pT1b (SM1), ly(-), v(-), pHM1, pVM0, pR1 (**Fig. 4**).

On the second postoperative day, he developed fever and increased sputum volume, which was diagnosed as coexisting aspiration pneumonia. Sulbactam sodium/ampicillin sodium were administered, and intraoral drainage was performed. Water intake was started on the fourth day, and meals were restarted on the eighth day.

On the 16th day, he had recovered and was discharged. Additional surgical resection and chemoradiation of the cervical esophageal cancer were considered, but the patient felt weak after the total gastrectomy. He thus declined highly invasive treatment and chose to receive chemotherapy alone. Chemotherapy with a combination of 5-fluorouracil and cisplatin (FP therapy) was started 2 months after surgery but was discontinued after 2 courses, at the request of the patient. His vitamin B12 deficiency anemia worsened because of nutrient malabsorption caused by the gastric resection and prior excessive alcohol intake. It has been 1.2 years since the ELPS/ESD, and he has experienced no recurrence.

Discussion

Hypopharyngeal cancers are commonly detected at an advanced stage after onset of subjective symptoms such as throat pain. The 5-year survival rate for such cancers is poor: 30% to 40%[1–3]. Surgery and radiation therapy for advanced hypopharyngeal cancers can greatly impair QOL. Because of recent advances in NBI magnifying endoscopy, pharyngeal and esophageal cancers are 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 selected.

ELPS—a procedure in which forceps and an electrical scalpel are inserted through the mouth to perform endoscopy-assisted submucosal separation—was conceived of and developed by Omori et al. in 2004[4,5] as a technique to treat superficial pharyngeal cancer. After intratracheal intubation under general anesthesia, the 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 superior to the head of the patient and first mark 1-2 mm outside the boundary of the lesion with an electrical scalpel. Next, an epinephrine-saline solution is injected locally, and a circumferential incision is made 1-2 mm outside the marking. Countertraction is applied with forceps, to separate the submucosa, and the lesion is resected en bloc[6].

Procedural complications of ELPS include hemorrhage, postoperative laryngeal edema, stenosis and dysphagia, vocal cord injury, postoperative transient vocal cord paralysis, subcutaneous emphysema, mediastinal emphysema, mediastinitis, and mediastinal abscess due to perforation[7]. The respiratory status of our patient was stable, even immediately after extubation; neither airway constriction nor hoarseness was observed. We thus determined that his condition was manageable in the general ward. However, on postoperative Day 2, he was diagnosed with aspiration pneumonia when saliva accumulation was noted in his mouth. The aspiration pneumonia resolved after antibiotic administration and intraoral drainage, and his oral intake resumed. He did not have dysphagia or aspiration, and aspiration pneumonia did not recur. These findings suggest that postoperative cicatricial stenosis of the hypopharynx had not preceded the aspiration pneumonia. We therefore concluded that the aspiration pneumonia was caused by impaired saliva swallowing associated with transient postoperative edema in the region from the hypopharynx to the cervical esophagus.

Kishimoto et al.[7] reported the safety, outcomes, and feasibility of ELPS for patients 75 years or older. No local recurrence was noted in the 19 patients, although 4 had positive margins. Postoperative aspiration pneumonia occurred in 2 patients with suspected invasion of the muscle layer but was safely managed. These results suggest that the oncological outcomes and safety of endoscopic resection are acceptable for vulnerable patients.

Pharyngeal cancer and esophageal cancer often occur as multiple or double cancers that develop in a metachronous manner. The risk factors are believed to include high alcohol consumption, a long history of cigarette smoking, and partial ALDH2 deficiency[8]. Few successful cases of simultaneous endoscopic resection of superficial pharyngeal and esophageal cancers have been reported, and the safety and effectiveness of the procedure are not well understood[9,10].

In the present case, we succeeded in simultaneously, and safely, resecting superficial hypopharyngeal and esophageal cancers by using ELPS and ESD. The pathological diagnosis was pT1b (SM1), pHM1 in an esophageal specimen. However, tumor cells infiltrated the submucosal layer at only one point, and no vessel invasion was found. The 2017 Guideline for Diagnosis and Treatment of Carcinoma of the Esophagus recommends additional treatment for pT1b cancer after endoscopic resection[11]. However, our patient declined highly invasive therapy such as surgery and chemoradiotherapy. Although the patient has not developed a recurrence, close observation is required.

When treating a patient with risk factors of pharyngeal or esophageal cancer, it is particularly important to check for the presence of double cancer before choosing a treat-

ment approach, and equally important to maintain observation during post-treatment follow-up, to detect metachronous double or multiple cancers. It is anatomically difficult to observe the area from the pharynx to the cervical esophagus with current endoscopy methods. The "trumpet maneuver" for observing the pharynx, proposed by Kawada et al., may be useful. A fora-wide view of the pharynx is obtained by inserting an endoscope into the nose and making the patient exhale strongly, so as to inflate the cheeks while the mouth is closed. If we can detect double cancers earlier 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 upper endoscopy, we believe that endoscopic and simultaneous resection of such double cancers will be a feasible option that helps maintain QOL.

Conclusion

Simultaneous ELPS and ESD was used to treat superficial cancers of the hypopharynx and esophagus. A postoperative complication was successfully managed and QOL was maintained after treatment.

Conflict of Interest: The authors declare no conflicts of interest.

References

1. Laranne J, Bäck L, Koivuneu P, Rukkila M, Rulkkinen J, Grénman R. Hypopharyngeal carcinoma in Finland from 1990-1999. Eur Arch Otorhinolaryngol. 2005;262:374–8.
2. Ferlito A, Shaha AR, Buckley JG, Rinaldo A. Selective neck dissection for hypopharyngeal cancer in the clinically negative neck: should it be bilateral? Acta Otolaryngol. 2001;121:329–35.
3. Togashi T, Sato Y, Kai R. [Treatment of hypopharyngeal cancer]. J Niigata Cancer Center Hospital. 2014;53:39–44. Japanese.
4. Omori T, Yokoyama A, Tagawa T, Sato Y. Endoscopic mucosal resection for superficial oropharyngeal and hypopharyngeal cancers. Japan Broncho-esophag Soc. 2004;55:133.
5. Kawakubo H, Omori T, Ando A, Sato Y, Sugiura J, Yokoyama K. Clinical outcome of treatment for superficial carcinoma of the oropharynx and the hypopharynx. Stomach Intestine. 2010;45:265–81.
6. Kawakubo H, Omori T, Nakamura R, Takeuchi Y, Kitagawa Y. Endoscopic laryngo-pharyngeal surgery (ELPS) for superficial carcinoma of the pharynx and cervical esophagus. Gastroenterol Endosc. 2014;56:64–70.
7. Kishimoto Y, Harada H, Funakoshi M, et al. Endoscopic laryngo-pharyngeal surgery for elderly patients. Auris Nasus Larynx. 2019;46:279–84.
8. Yokoyama A, Omori T, Yokoyama T. Alcohol and aldehyde dehydrogenase gene polymorphisms and multiple cancers associated with esophageal squamous cell carcinoma in Japanese alcoholics. Stomach Intestine. 2003;38:339–48.
9. Kawada K, Sugimoto T, Okada R, et al. A case of simultaneous triple primary cancers of the hypopharynx, esophagus, and stomach that were dissected by endoscopic laryngo-pharyngeal surgery combined with endoscopic submucosal dissection. Open J Gastroenterol. 2018;8:94–102.
10. Nakayama M, Katada C, Mikami T, et al. A clinical study of transoral pharyngectomies to treat superficial hypopharyngeal cancers. Jpn J Clin Oncol. 2013;43:782–7.
11. The Japan Esophageal Sosicety. Guideline for diagnosis and treatment of carcinoma of the esophagus 2017. Bunkyo-ku, JP: Kanehara Shuppan; 2017. p. 16–7.

(Received, March 31, 2019)
(Accepted, April 20, 2020)
(J-STAGE Advance Publication, May 30, 2020)