

A Case of Simultaneous Triple Primary Cancers of the Hypopharynx, Esophagus, and Stomach Which Were Dissected by Endoscopic Laryngo-Pharyngeal Surgery Combined with Endoscopic Submucosal Dissection

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Abstract

A 65-year-old man was admitted to our hospital following 6 months of dysphagia. At first, conventional endoscopy showed a reddish and depressed lesion in the stomach and an elevated lesion in the posterior wall of the hypopharynx. An endoscopic biopsy showed adenocarcinoma in the stomach, and squamous cell carcinoma in the hypopharynx. On the further examination, trans-nasal endoscopy with narrow band imaging (NBI) was performed. During the trumpet maneuver, a huge protruded lesion was observed and it reached to the orifice of the esophagus. Other superficial lesion located at left pyriform sinus was detected by NBI system as brownish area with brown dots. Furthermore, superficial esophageal cancer in the cervical esophagus was detected. Finally, 4 carcinomas in upper gastrointestinal tract were detected. Among them, the hypopharyngeal cancer was the most advanced (T3N0). The patient hoped to preserve his voice and swallowing function, endoscopic laryngo-pharyngeal surgery (ELPS) was performed for the hypopharyngeal cancer. Endoscopic mucosal resection (EMR) was performed for the esophageal cancer, and Endoscopic submucosal dissection (ESD) was performed for the gastric cancer. Under collaboration between a head and neck surgeon and an endoscopist, the tumor was resected *en-bloc*. The histopathological find-

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ings of hypopharyngeal cancer were squamous cell carcinoma, subepithelial invasion, 29 × 28 × 4.2 mm. The others were diagnosed as mucosal cancers. The patient is currently alive with no recurrence at 28 months after the surgery; there is no stricture at the cervical esophagus. Endoscopic laryngopharyngeal surgery for the tumor of pharyngo-esophageal junction can provide a less invasive treatment.

Keywords

Endoscopic Laryngopharyngeal Surgery, Hypopharyngeal Cancer, Multiple Primary Cancer, Trumpet Maneuver, Endoscopic Submucosal Dissection

1. Background

Recently, multiple primary malignant cancers in the same patient frequently have been found because of the advancing age of patients and improvements in the diagnostic tool in identifying early stage mucosal cancer of the head and neck. Synchronous and metachronous occurrence of squamous cell carcinomas within the head and neck region is well known as field cancerization [1] [2] [3]. Most cases of hypopharyngeal cancer are detected at an advanced stage, and require extensive treatment and are usually associated with a loss of function of swallowing or speaking. Several reports [4] [5] [6] have indicated the usefulness of narrow band imaging (NBI) improving the detection of superficial hypopharyngeal cancer. However, circumferential observation of the hypopharyngeal-mucosa is difficult during conventional endoscopy due to its anatomically closed nature. We previously reported that the utility of trans-nasal endoscopy using the trumpet maneuver for precise inspection before treatment [7] [8]. We here in report a case of simultaneous triple primary cancers of the hypopharynx, esophagus, and stomach which were dissected by Endoscopic laryngopharyngeal surgery (ELPS) combined with Endoscopic submucosal dissection (ESD).

2. Case Presentation

The patient was a 65-year-old man with dysphasia as the chief complaint. He had a heavy drinking career and also had some history of smoking. He had nothing remarkable in his family history. He had an anamnesis of the enlargement type cardiomyopathy. From around July 2015, he visited at the clinic near his home, but he was diagnosed as having no abnormality. From September 2015, the dysphagia progressed to the extent that he was unable to tolerate solid foods. He was admitted to our hospital. At first, conventional endoscopy showed a reddish and depressed lesion in the stomach (Figure 1) and an elevated lesion in the posterior wall of the hypopharynx (Figure 2). An endoscopic biopsy showed adenocarcinoma in the stomach, and squamous cell carcinoma in the hypopharynx. On the further examination, trans-nasal endoscopy with narrow

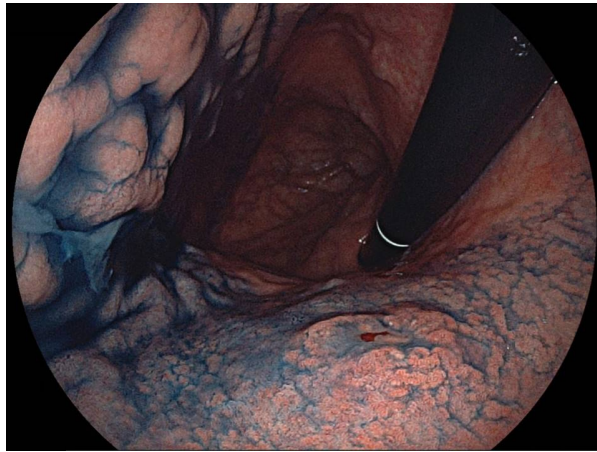


Figure 1. The early gastric cancer detected by conventional endoscopy with indigo carmine.

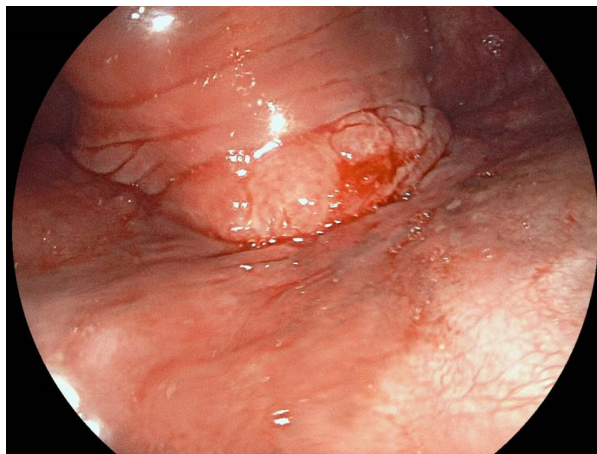


Figure 2. The protrude lesion was observed by conventional endoscopy. The distal side of the lesion was invisible.

band imaging (NBI) was performed. We have routinely performed the trumpet maneuver using trans-nasal endoscopy for patients with esophageal cancer since 2009, using the following procedure.

First, the patient was asked to bow his head deeply. We then placed a hand on the back of his head and pushed it forward. Then, he was asked to lift his chin as far as possible. After inserting the ultrathin endoscope (GIF-290N, Olympus.co., Tokyo, Japan) via the nose, the patient is asked to blow hard and puff the cheeks while the mouth remains closed (trumpet maneuver). The image of the hypopharynx with trans-nasal endoscopy using NBI system is shown in **Figure 3(a)**. The distalside of the tumor was invaded to the cervical esophagus (Video: <https://www.youtube.com/watch?v=H2YfgeyEwr0&feature=youtu.be>) Other superficial lesion located at left pyriform sinus was detected by NBI system as brownish area with brown dots (**Figure 3(b)**). Furthermore, superficial esophageal cancer in the cervical esophagus was detected as brownish area with brown dots (**Figure 4**). Finally, 4 carcinomas in upper gastrointestinal tract were detected.

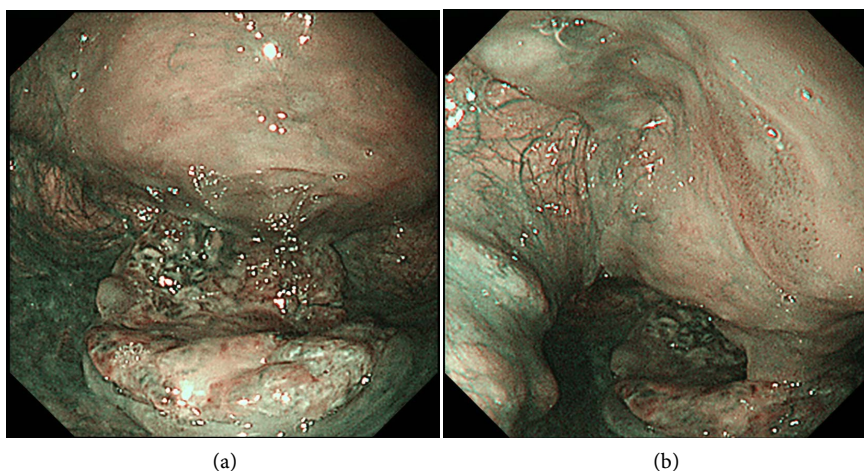


Figure 3. (a) The huge and protruded lesion was observed by trans-nasal endoscopy with NBI system using trumpet maneuver. The distal side of the tumor was invaded to the cervical esophagus; (b) The Brownish area was observed at the left piriform sinus with NBI system.

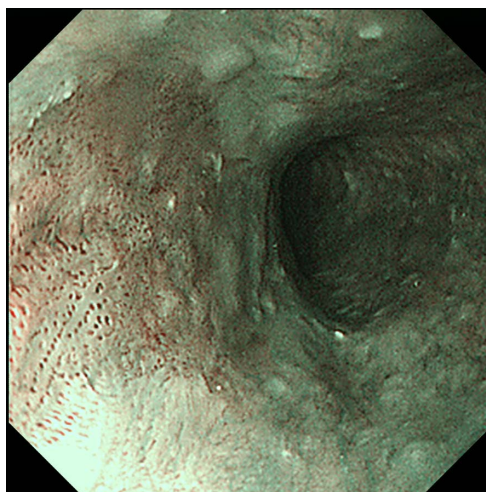


Figure 4. The cervical esophageal cancer detected by transnasal endoscopy with NBI system.

Computed tomography revealed hypertrophy of the wall of the hypopharynx, and no lymph nodal metastasis, or distant metastasis. The prognosis was based on advanced hypopharyngeal cancer (T3N0M0, Stage III). The patient's treatment method was decided after the discussion with head and neck surgeon and gastroenterologist. He was recommended to undergo chemo-radiotherapy. However, his performance status was not so good, he refused invasive treatments and hoped to preserve his voice and swallowing function. At first, we decided to perform endoscopic resection for hypopharyngeal cancers and superficial esophageal cancer cooperated with head and neck surgeon.

3. Therapeutic Procedure

Endoscopic laryngopharyngeal surgery is a hybrid of gastrointestinal endoscopic

treatment and head and neck surgery [9]. The endoscope is passed through the nasal route, and the surgeon inserts the curved forceps and the electric knife through the mouth. Endotracheal intubation is administered under general anesthesia, and the larynx is lifted using a Sato's curved laryngoscope (Nagashima Medical instruments Company, Ltd., Toyo, Japan) developed by Sato *et al.*, so we can get a good, wide working space. At first iodine staining was performed, we could recognize the lateral margin of the tumor. Then the margin was marked using electric knife in coagulation mode.

After the marking, inject a solution of epinephrine (0.02 mg/ml), indigo carmine, and saline into the subepithelial layer beneath the lesion. After the injection, make the cutting 2 mm outside of the marking. At the distal side of the hypopharyngeal cancer and the esophageal cancer, the electric knife couldn't reach, so it was difficult for the head and neck surgeon to perform the operation alone. Endoscopic mucosal resection (EMR) for the superficial cervical esophageal cancer was performed. Then an endoscopist dissected the distal margin using the electric knife inserted through a flexible endoscope (Endoscopic submucosal dissection technique). At the proximal side of the hypopharyngeal tumor, the cutting and dissection procedure was performed combination of the trans-orally inserted curved forceps in one hand and the electric knife in the other hand (**Figure 5**). Finally, the tumor was resected en bloc. The superficial lesion located at left piriform sinus was dissected by ELPS procedure. All the tumors were resected one piece (**Figure 6**). The total operation time was 80 min. The patient was extubated immediately after surgery. The fasting period was 5 days after surgery, and the postoperative hospital stay was ten days. 2 months later, the gastric cancer was dissected by endoscopic submucosal dissection. All specimens were microscopically evaluated (**Table 1**). The histopathological finding of the main tumor was squamous cell carcinoma, 29 × 28 mm, subepithelial invasion (the tumor thickness was 4200 μm), and a negative lateral and

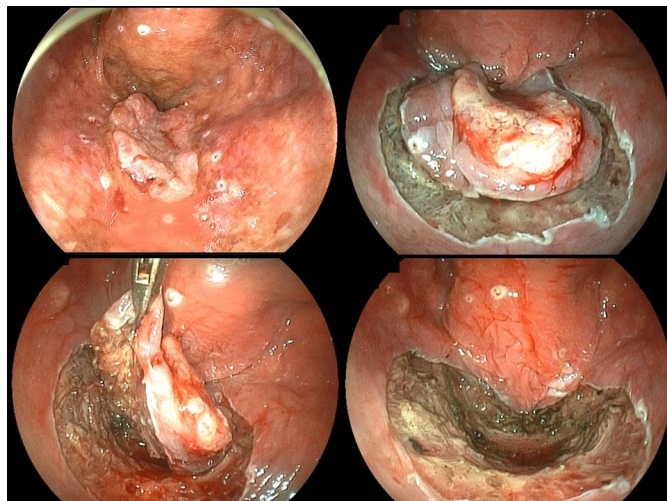


Figure 5. The hypopharyngeal cancer was dissected by endoscopic laryngopharyngeal surgery.

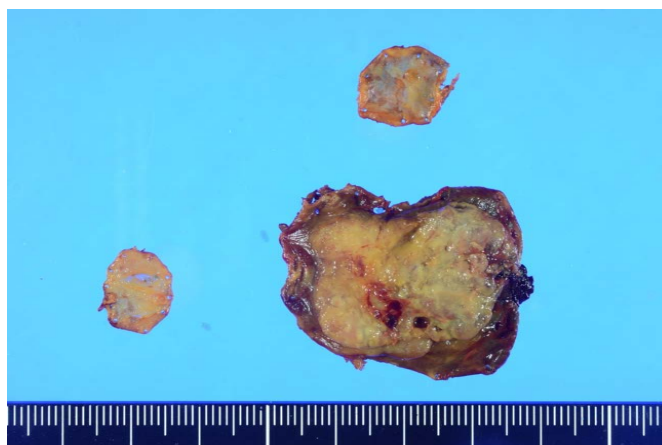


Figure 6. 3 resected specimens (two hypopharyngeal cancers, one esophageal cancer).

Table 1. Histopathological findings.

Location	Size (mm)	Macroscopic type	Depth of invasion	Histopathological findings	Treatment
Hypopharynx ①	29 × 28	0 - I	Sep (4200 μm), ly0, v1	Squamous cell Carcinoma	ELPS + ESD
Hypopharynx ②	8 × 7	0 - II b	Carcinoma <i>in situ</i>	Squamous cell Carcinoma	ELPS
Cervical Esophagus	8 × 8	0 - II c	Microinvasion	Squamous cell Carcinoma	EMR
Stomach	7 × 5	0 - II c	Mucosal cancer	Adenocarcinoma (tub 1 - 2)	ESD

vertical margin (**Figure 7**). During the follow-up period of 28 months, there is no stricture at the cervical esophagus (**Figure 8**). The phonation and swallowing functions were preserved. Close collaboration between head and neck surgeons and endoscopists can provide good results in treating tumors of the pharyngo-esophageal junction.

4. Discussion

Regarding the theory of the development of multiple primary cancers, Slaughter *et al.* [1] proposed the field cancerization theory that explained the concept of multicentric origin, and this theory is still accepted. It has been reported that the application of magnifying endoscopy with the NBI system drastically changes the diagnostic strategy for the early detection of early head and neck cancers [4] [5] [6]. However, some areas are difficult to observe with conventional endoscopy. We previously reported the utility of trans-nasal endoscopy using the trumpet maneuver for precise inspection before the treatment [7].

In this case, we can detect the superficial cervical esophageal cancer, and 2 hypopharyngeal cancer (type 0 - I, type 0 - II b) using trans-nasal endoscopy with NBI system.

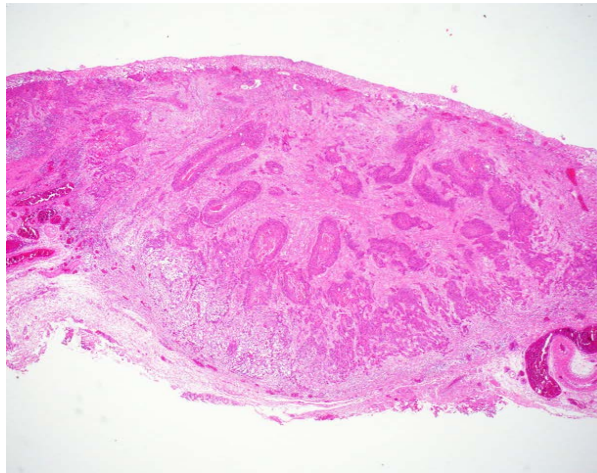


Figure 7. A histopathological examination revealed a diagnosis of invasive squamous cell carcinoma with negative lateral and vertical margin. The tumor thickness was 4200 μm .

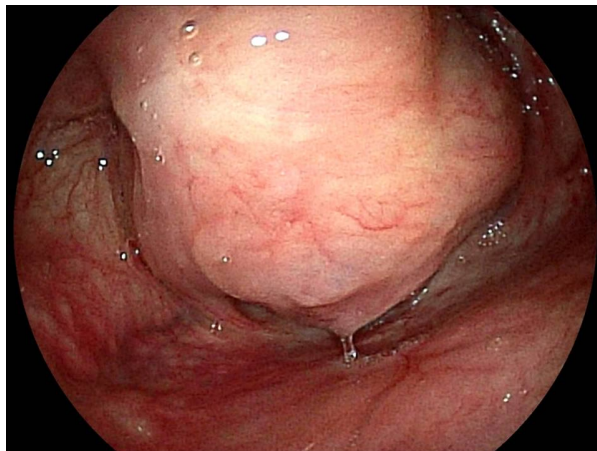


Figure 8. At 28 months after treatment, no local recurrence was observed.

Trans-oral surgery is becoming a major strategy in the treatment of laryngo-pharyngeal cancer [10]. If the lesion was diagnosed as carcinoma *in situ* or carcinoma with invasion to the subepithelial layer, Endoscopic laryngo-pharyngeal surgery was indicated as a minimally invasive treatment. It has been reported that the ratio of subepithelial invasion or muscular invasion in type 0 - I were 100% [11]. In determining the treatment strategy, the stage and location of the tumor and the general status of the patient should be considered. The 0 - I located at hypopharyngeal lesion of the present case seems to have a deep subepithelial invasion. The indication for ELPS was thought to be difficult.

Chemo-radiotherapy is widely performed at present but is associated with a high frequency of early and late toxicities [12]. Total pharyngo-laryngo-esophagectomy is considered the most complicated and most invasive surgery for the gastro-intestinal tract [13].

We have experienced a case of type 0 - I located at the pharyngo-esophageal

junction dissected by ELPS with ESD before [14]. In Japan, most cases of superficial squamous cell carcinoma located at the cervical esophagus are treated by endoscopically, so we selected the endoscopic treatment for both hypopharyngeal and cervical esophageal cancer. In this case, we could easily perform surgery without any complications. After endoscopic resection for superficial pharyngeal cancer, additional treatments such as radiation therapy or radical resection may be needed. We use a “resect and watch strategy [15]”, it means that observe until development of secondary diseases, including local recurrence, neck lymph node metastasis, and metachronous pharyngeal cancer.

The follow-up examinations after treatment, included cervical ultrasound and the measurement of his tumor marker levels every three months, and computed tomography every six months. Balloon dilation was not required. The patient is currently alive with no recurrence at 28 months after the surgery. More cases and longer follow-up periods will be required to obtain conclusive findings, and future studies will need to determine the indications of this treatment.

5. Conclusion

We have been experienced a case of simultaneous multiple cancers located at hypopharynx, cervical esophagus, stomach cured by endoscopic treatment. It is a less invasive treatment than conventional surgery and is becoming a major strategy in the treatment of superficial pharyngeal cancer.

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