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Case Report

A Case with Laryngeal Cartilage Necrosis after Trans Oral Surgery for Superficial Squamous Cell Carcinoma

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ABSTRACT

In recent years, Trans oral surgery (TOS) for superficial squamous cell carcinoma of the oropharynx and hypopharynx has frequently been performed in Japan. TOS offers benefits to patients, such as minimal invasiveness and a shorter treatment period. We sometimes encounter complications associated with TOS and report herein a rare case with a severe complication of laryngeal cartilage necrosis after TOS.

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Introduction

A high-magnification endoscope was first utilized for detecting superficial esophageal cancer by Inoue *et al.* [1]. This method has now been applied to head and neck cancer. Moreover, the use of narrow-band imaging (NBI) has started allowing the detection of superficial squamous cell carcinoma of the oropharynx, hypopharynx and larynx by Muto *et al.* [2]. NBI enables the detection of superficial squamous cell carcinoma, which is capable of being resected using a trans-oral endoscopic approach with minimal invasiveness [2-5]. Diagnostic and therapeutic methods using both NBI and endoscopic resection have provided a general method for detecting and treating superficial squamous cell carcinoma (SCC) in the head and neck region beyond the esophagus [6]. Trans oral surgery (TOS) confers major advantages of decreased invasiveness and a shortened treatment period compared to radiotherapy or open surgery for patients with early invasive cancer. TOS has thus proven greatly beneficial in decreasing the treatment burden imposed on patients. However, unexpected events that were not anticipated before TOS sometimes occur in patients after TOS. We report herein a rare complication that we encountered in association with TOS.

Case Presentation

The patient was a 52-year-old man with a history of frequent treatments such as endoscopic resection and chemoradiotherapy for multiple hypopharyngeal and esophageal cancers (Table 1). The patient had not shown any symptoms prior to the detection of a lesion in the hypopharyngeal region. The lesion was recognized as a mild superficial irregularity of the mucosa in the postcricoid area of the hypopharynx under routine surveillance using upper gastrointestinal endoscopy (GIE). In addition, we performed GIE using NBI with magnifying endoscopy for the purpose of acquiring detailed findings for the pharyngeal region (Figure 1). Histopathological examination of a biopsy specimen of the lesion revealed SCC. Written informed consent for endoscopic local resection and TOS was obtained, and TOS was performed under general anaesthesia. A curved-type rigid laryngoscope (Nagashima, Tokyo, Japan) was inserted to widen the pharyngeal space. Conventional endoscopy showed a superficial protrusion with mild mucosal irregularity in the postcricoid area (Figure 2), appearing as a brownish area on NBI endoscopy (Figure 2).

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Table 1: Past therapeutic histories.

Past therapeutic histories				
	Time before this therapy	portion		Therapy
Esophagus	12years ago	Mt	cT2N1M0	CRT(CDDP+5-FU)
	6.5years ago	Mt	pTis	EMR/ESD
	6.0years ago	Ce	pTis	EMR/ESD
	3.5years ago	Mt and Lt	pTis	EMR/ESD
	2.0years ago	Ce	pTis	ESD
Pharynx and Larynx	6.8years ago	Right-PS	pT1	ESD
	6.5years ago	Right-PS	pT1	ESD
	4.0years ago	PW	pTis	ESD
	2.8years ago	Left-PS	pTis	ESD
	2.2years ago	Right-PS, Right-arytenoid, PW	pTis	ESD
	1.8years ago	epiglottis (left side)	pTis	ESD

Ce: Cervical Esophagus; Mt: Mid Thoracic; Lt: Lower Thoracic; PS: Pyriform Sinus; PW: Posterior Wall; CRT: Chemo-Radio Therapy; EMR: Endoscopic Mucosal Resection; ESD: Endoscopic Submucosal Dissection.

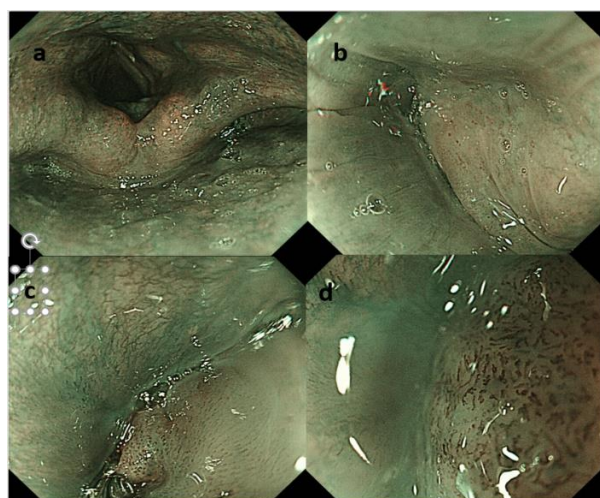


Figure 1: Endoscopic findings of hypopharynx **a)** An overview with NBI, irregular brownish elevated lesion was detected at postcricoid. **b)** The lesion was spread to the left pyriform sinus, and it was clarified with NBI. **c)** The lesion was revealed as well demarcated brownish area with NBI. **d)** The lesion showed dense microvascular irregularity under NBI with magnification.

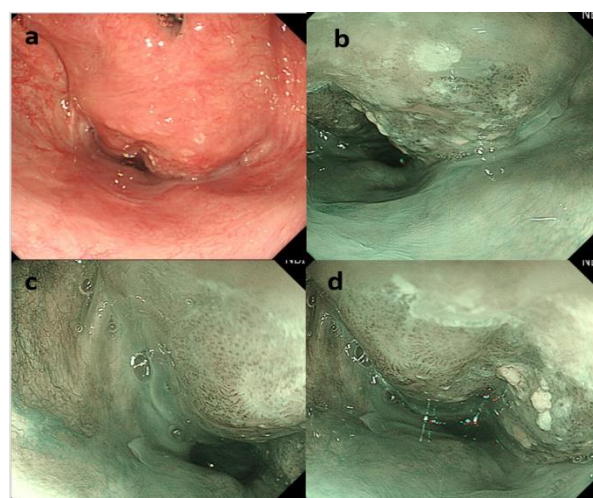


Figure 2: Endoscopic findings of hypopharynx under general anaesthesia. **a)** An overview with conventional light, irregular reddish elevated lesion was detected at post-cricoid. **b)** The lesion was revealed as well demarcated brownish area with NBI. **c)** The lesion was spread to the left pyriform sinus, and it was clarified with NBI. **d)** The lesion was invaded to cervical esophagus, and dense irregular microvascular were appeared under NBI with magnification.

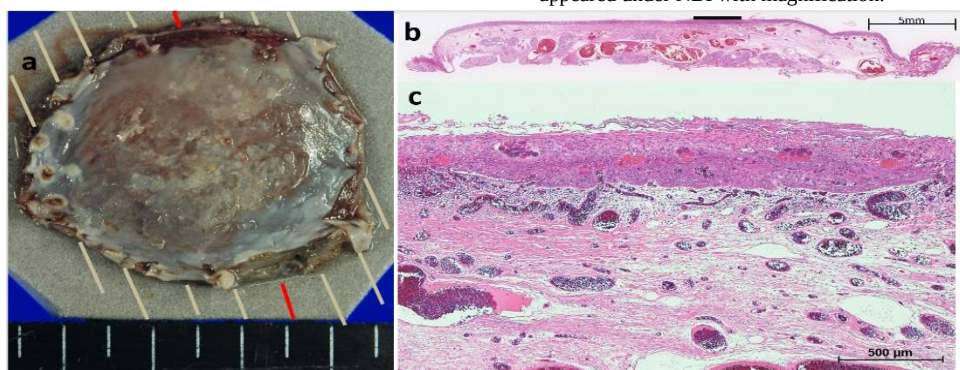


Figure 3: Pathological findings of this case. **a)** The macroscopic photo of the resected specimen fixed with formalin. **b)** The microscopic photo of the section at the red line in Figure 3a without subepithelial invasion. **c)** The higher magnified microscopic photo of the same section as Figure 3b. The pathological diagnosis was squamous cell carcinoma *in situ*, pTis. The vascular infiltrations were not observed (ly0, v0), the horizontal margin was not determined, and the vertical margin was free (pHMX, pVM0). The pathological tumor size was 30x24mm, the macroscopic type was type0-IIa.

NBI and endoscopic iodine staining were used to confirm the extent of the lesion before TOS, and subsequently to verify the margins of

resection. A mucosal incision was then made around the lesion using an electrocautery. After making a circumferential incision around the

lesion, the lesion was completely dissected by exfoliating subepithelial tissue around the lesion with an electrocautery and a Maryland dissector. A superficial lesion measuring 39×37 mm was resected with sufficient margins. Severe laryngeal edema was present at the end of resection, so tracheostomy was performed to prevent airway obstruction. Histopathological diagnosis of the lesion was SCC *in situ* (Figure 3). Oral intake of liquid diet was started on postoperative day (POD) 3, the tracheostomy tube was removed on POD 7 once laryngeal edema had resolved, and the patient was discharged on POD 11. Although the patient did not show any symptoms in the head and neck region, a white-coated ulcer persisted in the postcricoid region and wound healing was delayed.

The patient complained of sudden respiratory discomfort on POD 50, and laryngeal edema was found to have recurred (Figure 4a). Emergency

tracheostomy was, therefore, performed. We identified an unhealed deep ulcer in the postcricoid region under GIE (Figure 4b) and noted a partial defect of the cricoid cartilage on computed tomography (CT) (Figure 4c). A biopsy specimen was subjected to histopathological examination to exclude the possibility of local recurrence, and the pathological diagnosis was granulation tissue. We instructed the patient to temporarily halt oral intake to rest the pharynx. We had not previously experienced laryngeal cartilage necrosis associated with TOS, and no reports in the literature appeared to give any clues to treatment. We tried re-biopsy from a smaller postcricoid ulcer under general anaesthesia on POD 78 (Figure 5). Histopathological examination of the biopsy specimen revealed tissue consisting of necrotic debris and granulation tissue. We also noted a mass protruding into the membranous wall of the trachea on CT performed on POD 100 (Figure 6). The mass consisting of granulation tissue formed by biopsy, resolved naturally by POD 158.

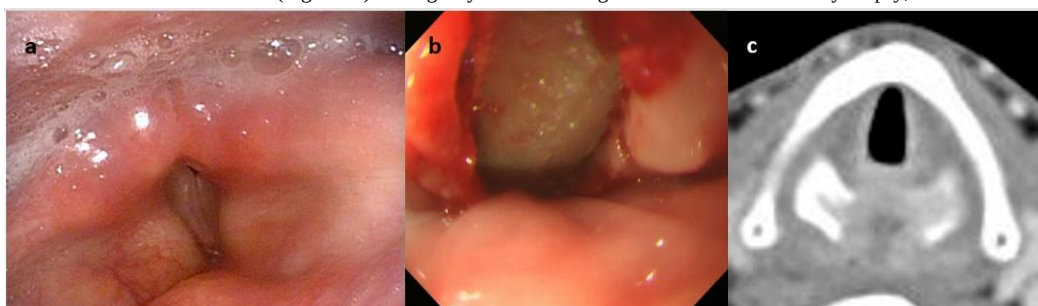


Figure 4: Endoscopic findings and image of computed tomography. **a)** Bilateral laryngeal palsy and stenosis of upper airway with laryngeal edema. **b)** Unhealed deep ulcer in the postcricoid region. **c)** Partial defect of the cricoid cartilage on CT.

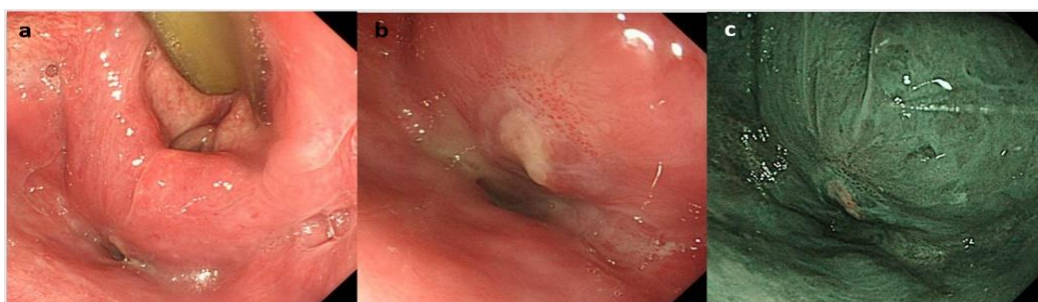


Figure 5: Endoscopic findings of hypopharynx under general anaesthesia. **a)** An overview with conventional light. **b)** Postcricoid area with smaller ulcer. **c)** Postcricoid area without microvascular irregularity under NBI.

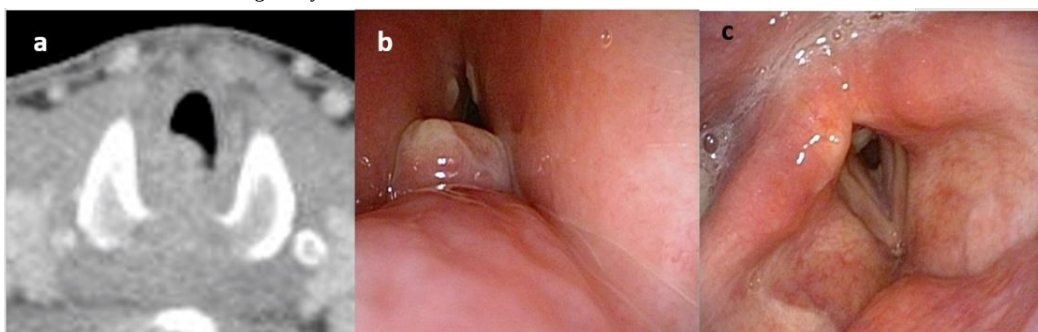


Figure 6: A mass protruding into the membranous wall of the trachea. **a)** Partial defect of the cricoid cartilage on computed tomography. **b)** A protruding mass (trans tracheal stoma view). **c)** A protruding mass (trans nasal view).

The final diagnosis was partial necrosis of the cricoid cartilage after TOS. The patient showed no laryngeal palsy, required no tracheal cannulation, experienced no recurrence of cancer and was able to resume eating a normal diet by 1.5 years postoperatively.

Discussion

Synchronous or metachronous overlap of cancers in patients with head and neck region is known as field cancerization. In fact, the overlap rate is 14.5% [7]. However, reports of patients receiving combined

multimodal therapies (surgery, endoscopic therapy, radiation therapy, chemotherapy) are extremely rare. TOS appears appropriate for cases such as this, where the patient has a past history of multiple hypopharyngeal and esophageal cancers. The present case reminds us of the hypothesis that a therapeutic history, including chemoradiotherapy and radiotherapy, may lead to partial necrosis of the cricoid cartilage. This patient had a history of various treatments, including chemoradiotherapy for esophageal cancer with an irradiation field covering the cervical esophagus, and endoscopic submucosal dissection (ESD) was performed in the pharynx five times. No original (i.e., untreated) mucosa of the pharynx or esophagus other than the postcricoid area was present at the time of this treatment. The postcricoid area was also anatomically peripheral in terms of blood supply [8]. Furthermore, endothelial damage in the pharynx and cervical esophagus was speculated to be caused by irradiation.

We performed wide resection of the postcricoid area, which led to injury to the esophageal mucosa at the junction between hypopharynx and cervical esophagus during the endoscopic operation. The postcricoid area took a prolonged time to heal due to inflammation and necrosis of the cricoid cartilage. We performed tracheostomy and instructed the patient to temporarily halt oral intake in order to allow the pharynx to rest. The potential mechanisms underlying this case are shown in (Figure 7).

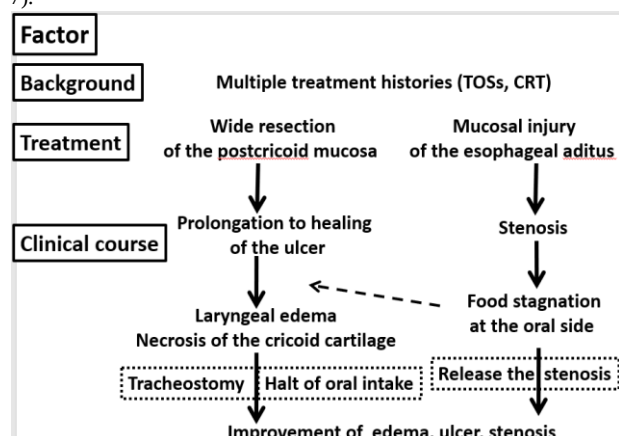


Figure 7: The plausible mechanism of this case.

A small number of reports have described complications associated with ESD for head and neck cancer, including postoperative bleeding, subcutaneous emphysema and laryngeal edema in the early period after ESD [9]. Complications in the late period have included mediastinal abscess and laryngeal necrosis [9, 10]. Patients with a history of radiation to the neck field appear more likely to experience late complications. Our patient overcame these complications with minimal damage from the partial necrosis because the radiation field was limited to the anal side of the cervical esophagus. We should pay close attention to patients with a history of multiple treatments, particularly those involving radiotherapy, to ensure complications are detected as soon as possible. The treatment strategy for necrosis of the laryngeal cartilage is rest and control of any bacterial infection. An advanced treatment option is hyperbaric oxygen therapy [11-13].

Conservative treatment was our first option, but total laryngectomy could be an option in cases where laryngeal necrosis has progressed. Necrosis of the laryngeal cartilage should be carefully distinguished

from recurrence by histopathological examination of biopsy specimens, and excessive surgical procedures such as total laryngectomy should be avoided. Correct and prudent diagnosis in closer cooperation with physicians and pathologists is very important. However, a limitation of this report is that it only involved a single case. Further multicenter studies are necessary to clarify the pathological mechanisms underlying cartilage necrosis by analysing a large number of patients with the same therapeutic history as the case presented in this report.

Conclusion

In conclusion, we should understand the presence of severe complications associated with TOS for head and neck SCC, such as laryngeal cartilage necrosis that we encountered in patients with a history of multiple therapeutic interventions. The postcricoid area is anatomically peripheral in terms of blood supply and should be treated with the utmost care.

Conflicts of Interest

None.

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