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Observation of the Pharynx to the Cervical Esophagus Using Transnasal Endoscopy with Blue Laser Imaging

Kenro Kawada, Tatsuyuki Kawano, Taro Sugimoto, Toshihiro Matsui, Masafumi Okuda, Taichi Ogo, Yuuichiro Kume, Yutaka Nakajima, Katsumasa Saito, Naoto Fujiwara, Tairo Ryotokuji, Yutaka Miyawaki, Yutaka Tokairin, Yasuaki Nakajima, Kagami Nagai and Takashi Ito

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Abstract

Background In 2014, the new transnasal endoscopy with Blue laser Imaging (BLI) has been developed. Aim We present the usefulness of the observation of from the pharynx to the cervical esophagus using transnasal endoscopy with BLI. Patients and Methods This study was conducted between June 2014 and October 2014. During this period, 70 consecutive patients (60 men, 10 women; mean age 67.9 years old) with esophageal or head and neck cancer underwent endoscopic screening at the oropharynx and hypopharynx by transnasal endoscopy with BLI system We performed this endoscopic observation from oral cavity to pharynx before inserting into the cervical esophagus. The visibility of subsites of the hypopharynx and the orifice of the esophagus was evaluated. The extent of the view of hypopharyngeal opening was classified into 3 categories (excellent, good, poor). Then, the diagnostic accuracy of transnasal endoscopy with BLI system was estimated. Our screening is as follows. First, the patient is asked to bow their head deeply in the left lateral position. We put a hand on the back of the patient's head and push it forward. The patient is then asked to lift the chin as far as possible. In order to inspect the oral cavity, we insert an endoscope without a mouthpiece. After observation of the oral cavity, the endoscope was inserted through the nose. When the tip of the endoscope reached caudal to the uvula, the patient opened his mouth wide, stuck his tongue forward as much as possible and made a vocal sound like "ayyy". The endoscopist caused the endoscope to U-turn and observed the oropharynx, in particular the radix linguae (Intra-

oropharyngeal U-turn method). For examination of the hypopharynx and the orifice of the esophagus, the patient is asked to blow hard and puff their cheeks while the mouth remains closed (Trumpet maneuver). Results 8 elderly cases were excluded because they could not perform the adequate ballooning. Finally, 62 cases were investigated. The ballooning the pyriform sinus and posterior wall not only allows accurate assessment of the stretched pharyngeal mucosa but also gives a view of postcricoid subsite and the orifice of the esophagus. The wide endoscopic view of the pharynx was obtained in a series of the procedures (excellent=53/62, 85.4%; good=7/52, 4.5%; and poor=2/62, 7.6%). Among 70 patients, 6 superficial lesions (8.6%) at the oropharynx(n=1) and hypopharynx (n=5) were discovered with BLI system. Mucosal redness, a pale thickened mucosa, white deposits or loss of a normal vascular pattern, well demarcated areas covered with scattered dots are important characteristics to diagnose superficial carcinoma. Conclusion The more progress achieved in transnasal endoscopy rapidly in the last few years, it can improve for observing the blind area using trans-oral endoscopy, therefore the trans-nasal endoscope will be a standard tool for the screening of the upper gastrointestinal tract in the near future.

Keywords: Transnasal endoscopy, Blue laser imaging, Superficial pharyngeal cancer

1. Introduction

According to the “field cancerization” concept [1], head and neck cancer, especially pharyngeal cancer, frequently coexist with esophageal cancer. Recently several reports [2, 3] have indicated the possibility of applying narrow-band imaging (NBI) endoscopy with magnification to improve the detection of superficial pharyngeal cancer. Compared with conventional endoscopy, NBI results in dramatic improvements in the rate detection of superficial lesions and significant enhancement in visualizing the microvascular structure of the mucosal surface [4]. The superiority of NBI was also recently demonstrated in a multicenter randomized controlled trial in Japan [5]. As more progress has been achieved in the field of endoscopy, the number of superficial cancers in the head and neck region has increased.

However, some areas are difficult to observe with transoral endoscopy. In particular, achieving circumferential observation of the hypopharyngeal mucosa is difficult during conventional endoscopy due to the anatomically closed field, effects of the pharyngeal reflex and accumulation of saliva. On conventional endoscopic screening, the physician usually inserts the endoscope from the left pyriform sinus of the hypopharynx to the cervical esophagus, with a blind space in the posterior wall and postcricoid subsite of the hypopharynx as well as radix linguae. Therefore, detecting early signs of cancer in the blind space is difficult for gastrointestinal endoscopists. On the other hand, transnasal endoscopy may be performed comfortably due to attenuation of the gag reflex. In Japan, the transnasal endoscopy is a very popular procedure and can be performed without sedation. It has also been reported that transnasal endoscopy may be performed less invasive with respect to the cardiopulmonary function [6,

7], and the technique is considered to be more comfortable for the patient than conventional endoscopy.

Since we developed the pharyngolaryngeal observation method using transnasal endoscopy in 2009, we have constantly evolved the procedure in order to better detect carcinoma in the head and neck at earlier stages in cases often coexistent with esophageal cancer. In 2014, a new transnasal endoscopy device with Blue laser Imaging (BLI) was developed. The pharynx is the orifice of the gastrointestinal tract. In this article, we present the usefulness of observing the pharynx to the cervical esophagus using transnasal endoscopy with BLI.

2. Simple questionnaire

A complete medical history, including demographic and clinical data, was obtained prior to the endoscopy procedure. Selected patients constituting a high-risk group for pharyngeal carcinoma are beneficial targets of endoscopic surveillance. Epidemiological studies have detected several strong predictors for identifying persons at high risk for pharyngeal and esophageal squamous cell carcinomas. For example, alcohol drinking and tobacco smoking synergistically increase the risk of both cancers [8, 9], as does a reduced intake of greenish-yellow vegetables and fruits [10] and a low body mass index [11]. The presence of distinct esophageal iodine-unstained lesions and melanosis is also associated with a risk of cancer [12, 13], and alcohol consumption combined with inactive aldehyde dehydrogenase-2 (ALDH2) and less active alcohol dehydrogenase (ADH1B) enhances cancer risks in a multiplicative fashion [14, 15]. The detection of an enlarged mean corpuscular volume (MCV) [16], as induced by heavy drinking or smoking, a high level of acetaldehyde exposure, and/or poor nutrition, may be useful for identifying high-risk persons.

The results of a simple flushing questionnaire have been reported to predict the ALDH2 phenotype with a high accuracy [17].

3. Preparation

Transnasal endoscopy was performed without sedation. Prior to commencement of the procedure, each nasal cavity was sprayed with 0.05% naphazoline nitrate to induce vasoconstriction, followed by premedication with 100 mg of dimethylpolysiloxane and 10 000 U of pronase, with sodium bicarbonate to remove mucus and foam in the stomach. Nasal anesthesia was started by spraying a solution of 4% lidocaine into the nostril for three minutes, after which a swab covered with 8 % lidocaine spray was inserted into the deeper nasal cavity for two minutes. The patient was then placed in the lateral decubitus position to receive endoscopy. Antispasmodics such as scopolamine were not used for premedication.

3.1. Equipment

Recently, we applied a new transnasal esophagogastroduodenoscopy (EGD) device [EG-L580NW, Fuji Film, Tokyo, Japan] with the LASEREO system (a video processor (VP-4450:

FUJIFILM Co. Tokyo) including a light source (LL-4450; FUJIFILM Co. Tokyo)) under modification of the endoscopic technique for observing head and neck cancers and obtained excellent results. The endoscope is a transnasal endoscope that can provide high quality endoscopic images to be viewed on a monitor and digitally recorded with a wide field view of 140 degrees. The LASEREO system (FUJIFILM Co. Tokyo) is a novel endoscopic system employing a semiconductor LASER as a light source. This system is equipped with two LASERs with different wavelengths, one for white light sources (wavelength: 450 nm), and one for BLI (wavelength: 410 nm). The white light observation mode consists of a 450 nm LASER and fluorescence of white light phosphor, which is excited by a 450 nm LASER. The phosphor exists in the endoscope. BLI observation mode, which consists of a 410 nm LASER and feeble fluorescence light excited by a 450 nm LASER and is useful for acquiring mucosal surface information, including patterns of the surface blood vessels and structures. The endoscope allows for detailed observations in close view, as it has a focal length of 3 mm to achieve good endoscopic images. The endoscope also has a forceps with channel measuring 2.4 mm in diameter, which improves the ability to aspirate saliva and gastric juices and remove gastric mucus adhering to the tip of the endoscope. It has been reported that BLI is useful for making the diagnosis of colorectal tumors [18], or upper gastrointestinal lesions [19]. An abnormal microvascular pattern in brownish areas can be detected in most pharyngeal and esophageal cancers in the near view with white light images and clearly observed on BLI images. The color contrast of pharyngeal and esophageal cancers rises with BLI, resulting in useful screening result.

3.2. Endoscopic examinations-from the oral cavity to the oropharynx

Our screening procedure is as follows. First, the patient is asked to bow their head deeply in the lateral decubitus position. We then place a hand on the back of the patient's head and push it forward. The patient is then asked to lift the chin as far as possible (lateral sniffing position).

In order to avoid overlooking cancers in the floor of the mouth, soft plate and uvula, we first observe the oral cavity (Figure 1). and then insert the endoscope without a mouthpiece and subsequently observe the upper, lateral and posterior wall of the oropharynx while the patient sticks their tongue forward (Figure 2).

After observing the buccal cavity, further oropharyngeal observation is carried out with a retroflexed endoscope inserted via the nose. When the tip of the endoscope reaches the area caudal to the uvula, the patient opens their mouth wide and sticks their tongue forward as much as possible while making a vocal sound similar to "ayyy". The endoscopist causes the endoscope to make a U-turn (intra-oropharyngeal U-turn method) and observes the oropharynx, in particular the radix linguae. A schematic drawing of the procedure is shown in (Figure 3). We previously reported the usefulness of the intra-oropharyngeal U turn method [20]. One hundred and seventy-two patients underwent treatment with this method from April to October 2012. It was possible to observe all areas of the tongue from the radix linguae to the apex linguae, in 160 cases (93%) [21], and a frontal view of the papillae vallatae was obtained in all patients (Figure 4). After completing the intra-oropharyngeal U-turn method, the tip of the endoscope is inserted gently between the epiglottis and the tongue to observe the vallecula and the tonsil side of the epiglottis.

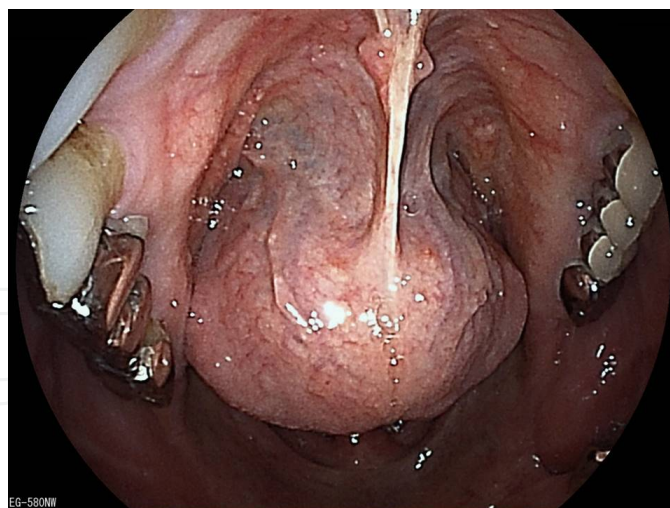


Figure 1. A view of the floor of the mouth through a trans-oral approach.

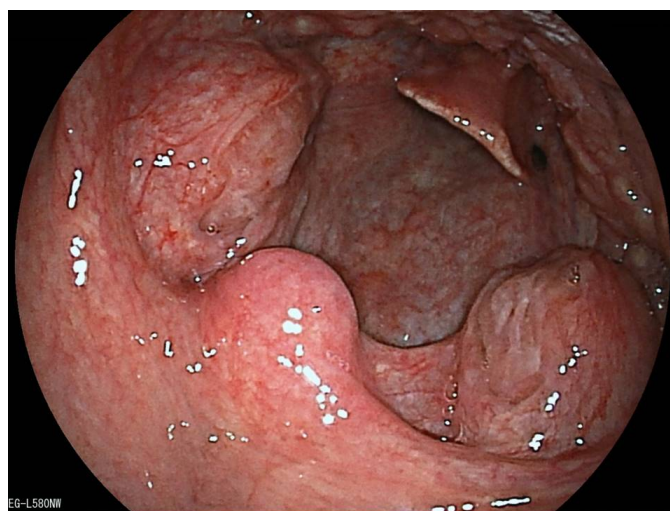


Figure 2. A view of the oropharynx through a trans-oral approach.

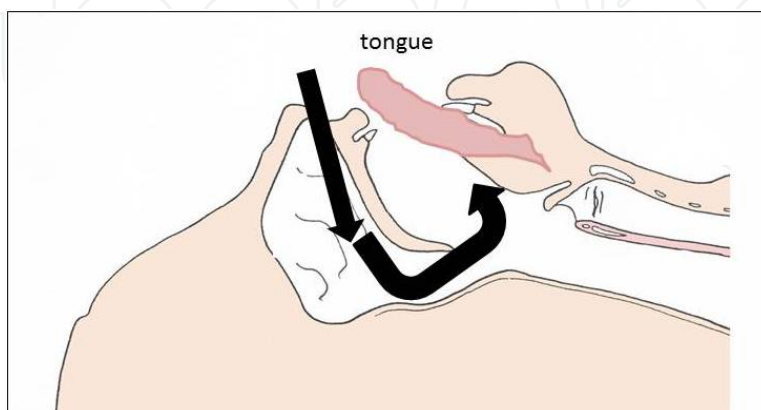


Figure 3. Schema of intra-oropharyngeal U-turn method.



Figure 4. A view of the radix linguae through a trans-nasal approach.

3.3. Endoscopic examination from the hypopharynx to the cervical esophagus

The vocal cords and right and left pyriform sinus should be observed (Figure 5). When the patient vocalizes, the vocal cords move to the anterior region, making observation of the pyriform sinus easier. The technique of esophagogastroduodenoscopy (EGD) has also been improved, although it is not possible to observe otorhinolaryngeal sites in some patients due to the gag reflex. The postcricoid subsite and orifice of the esophagus are especially difficult to visualize using flexible laryngopharyngoscopy. Several reports have suggested techniques for improving the view of the hypopharynx with a flexible fiber optic laryngoscope. Spraggs and Harris described a modified Valsalva technique involving the nose being squeezed shut by the examiner's hand while the patient attempts to blow through the obstructed nose [22, 23]. Other reports have described the trumpet maneuver [24], the anterior neck skin traction maneuver [25] or a combination of the two [26]. However, these maneuvers have not been attempted in conventional EGD due to the effects of the gag reflex.

Since we introduced the modified Valsalva maneuver using transnasal endoscopy in 2009 [27], a total of 94 superficial head and neck cancers were found in 70 patients using transnasal ESD over the last four years [28]. Furthermore, it has been reported the modified Valsalva maneuver using transnasal endoscopy is prospectively useful for detecting superficial pharyngeal cancer [29].

For the examination of the hypopharynx and orifice of the esophagus, the patient is asked to blow hard and puff their cheeks while keeping their mouth closed. The endoscopist pulls the patient's chin forward with the right hand, and the characteristics of the posterior wall of the hypopharynx and postcricoid subsite pharyngeal wall enable the pharyngeal mucosa to be stretched out and the postcricoid region (Figure 6) and orifice of the esophagus to be visualized in an open space. The transnasal BLI system enables clear visualization of the palisade vessels of the pharyngoesophageal junction (Figure 7). The total time required to perform the procedure is approximately two minutes. This technique is easy to perform and feasible in almost all high-risk patients. The endoscope is then passed into the cervical esophagus.

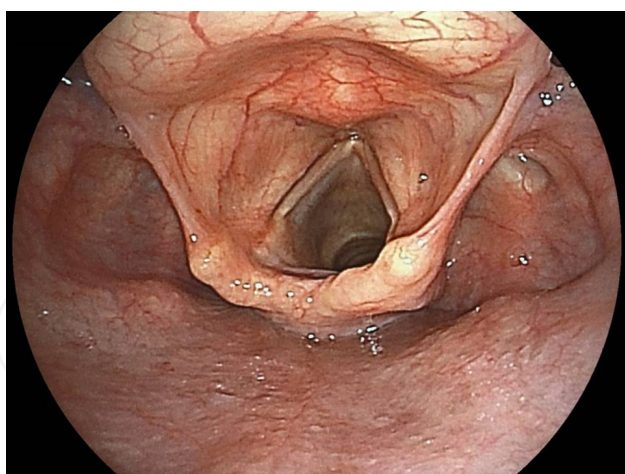


Figure 5. A view of the larynx and the hypopharynx.

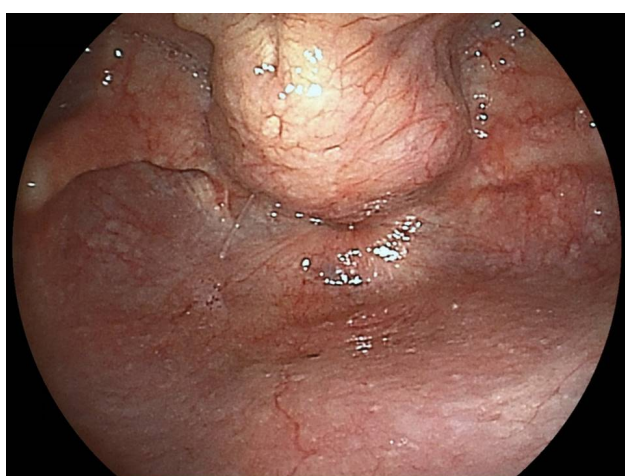


Figure 6. Transnasal endoscopy using trumpet maneuver improves the visualization of the hypopharynx and the pharyngoesophageal junction.

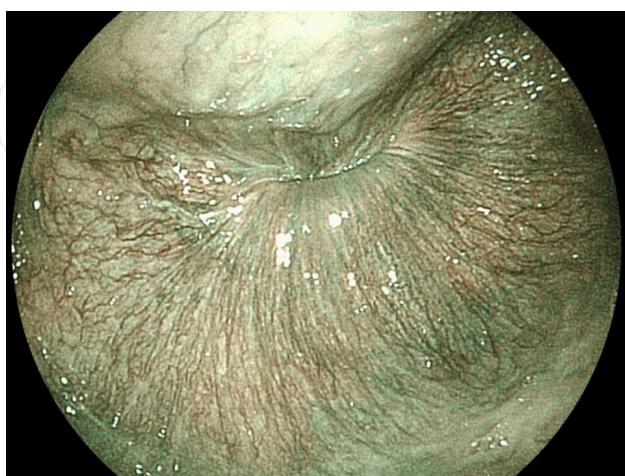


Figure 7. The endoscopic image of the pharyngoesophageal junction using Blue laser imaging (BLI).

4. Patients and Methods

This study was conducted between June 2014 and October 2014. During this period, 70 consecutive patients (60 males, 10 females; mean age: 67.9 years old) with esophageal or head and neck cancer underwent endoscopic screening of the oropharynx and hypopharynx using transnasal endoscopy with the BLI system at the Department of Esophageal and General Surgery, Tokyo Medical and Dental University. We performed endoscopic observation from the oral cavity to pharynx before inserting the endoscope into the cervical esophagus. BLI images were obtained on a color video monitor by pushing a fingertip control switch. The visibility of subsites of the hypopharynx and the orifice of the esophagus was evaluated, and the extent of view of the hypopharyngeal opening was classified into three categories (excellent, good, poor). The diagnostic accuracy of transnasal endoscopy with the BLI system was subsequently estimated. Two experienced endoscopists (K.K., N.F.) performed all of the examinations, using the same endoscope.

The examinations were recorded onto video cassettes. Written informed consent was obtained from all patients prior to the endoscopic examinations.

5. Results

Eight elderly patients were excluded due to inadequate ballooning. Finally, 62 patients were investigated. Ballooning of the pyriform sinus and posterior wall allows for both an accurate assessment of the stretched pharyngeal mucosa and provides a view of the postcricoid subsite and orifice of the esophagus.

A wide endoscopic view of the pharynx was obtained in a series of the procedures (excellent=53/62, 85.4%; good=7/52, 4.5%; and poor=2/62, 7.6%). Among the 70 patients, six superficial lesions (8.6%) at the oropharynx (n=1) and hypopharynx (n=5) were discovered with the BLI system (Table 1). Three lesions were located at the pyriform sinus and two lesions were located on the posterior wall of the pharyngoesophageal junction, which is the blind area on conventional screening. A representative lesion is shown in Figure 8. The hypopharynx was stretched according to the trumpet maneuver, which allowed us to detect a slightly depressed area. On BLI observation, a well demarcated brownish area was recognized, with scattered brown dots within the areas on a close view (Figure 9). The lesion was resected via endoscopic laryngopharyngeal surgery (ELPS). The area unstained with iodine was similar to the brownish area observed on BLI (Figure 10).

The histopathological examination revealed a diagnosis of squamous cell carcinoma with microinvasion beneath the epithelium (Figure 11).

In one case, superficial oropharyngeal cancer was located at the radix linguae (Figure 12), and the intra-oropharyngeal U-turn method was very effective for making the diagnosis.

Case	Sex	Age	Esophageal cancer	location	Macroscopic type	Size	Treatment	Tumor thickness
1	Male	72	Synchronous	PW	0-II a	21mm	ELPS	350µm
2	Female	56	Metachronous	PW	0-II c	12mm	ELPS	250µm
3	Male	69	Metachronous	rtPS	0-II b	※10mm	-	
4	Male	63	Synchronous	rtPS	0-II b	※15mm	-	
5	Male	66	Metachronous	ltPS	0-II b	※15mm	-	
6	Male	60	Metachronous	Oro	0-II c	※25mm	TORS	

PW=posterior wall of hypopharynx, rtPS= right piriform sinus
 lt PS=left piriform sinus, Oro=oropharynx, TORS=transoral robotic surgery
 ELPS=endoscopic laryngopharyngeal surgery ※=endoscopic findings

Table 1. The oropharyngeal and hypopharyngeal cancers detected by transnasal endoscopy with BLI.

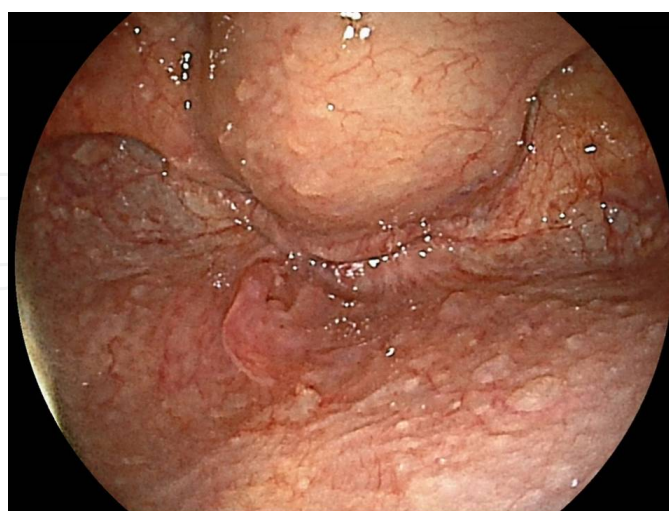


Figure 8. A slightly depressed lesion was observed in the posterior wall of the hypopharynx using the trumpet maneuver.

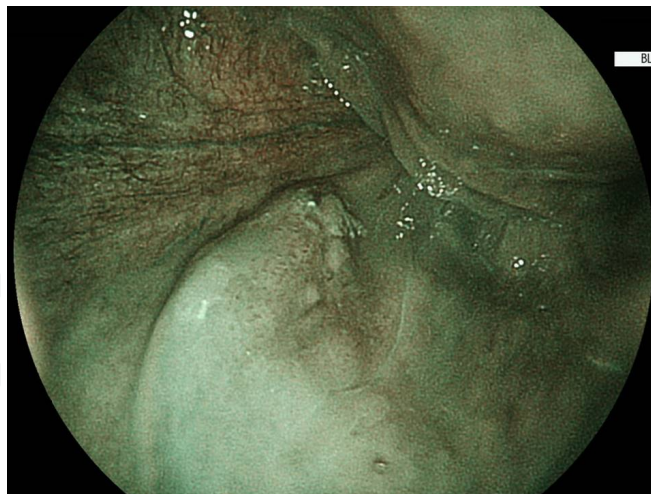


Figure 9. The endoscopic image using the BLI during the trumpet maneuver

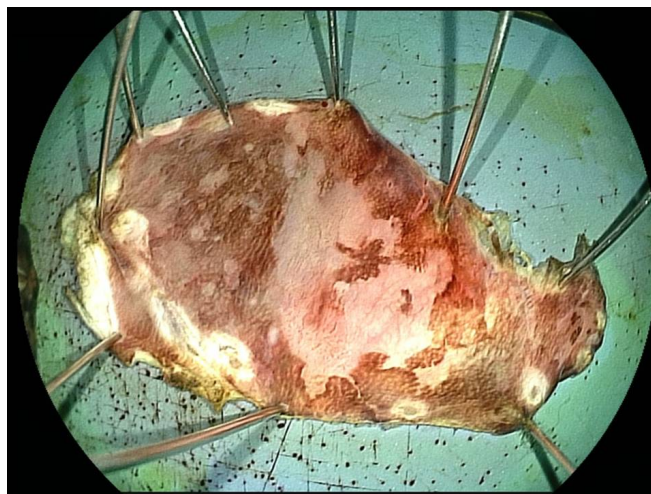


Figure 10. A macroscopic image of the resected specimen.

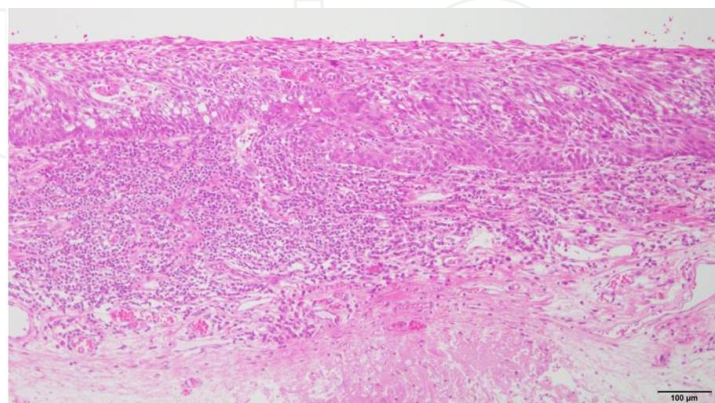


Figure 11. Histopathological examination revealed a diagnosis of squamous cell carcinoma with microinvasion beneath the epithelium.

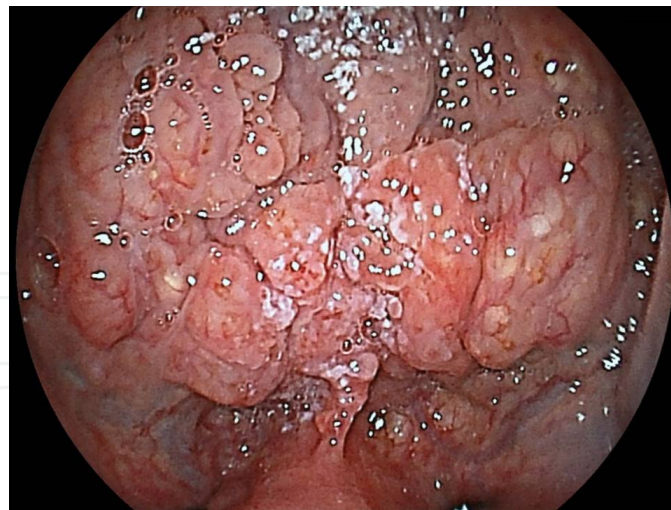


Figure 12. A case of superficial oropharyngeal cancer. The tumor observed using intra-oropharyngeal U-turn method.

5.1. Endoscopic features of superficial pharyngeal cancer

Recent advances in endoscopic procedures, such as magnifying endoscopy and the NBI system, have enabled precise observation of the oropharynx and hypopharynx [2, 5]. Mucosal redness, a pale and thickened mucosal appearance, white deposits and/or loss of the normal vascular pattern are important characteristics for diagnosing superficial carcinoma upon examination under white light (Figure 13). In addition, well demarcated areas covered with scattered dots observed on a closer observation of superficial microvascular structures and allows for the detection of a lesions at an earlier stages. The new transnasal endoscopy procedure with the BLI system enables physicians to easily observe the presence of scattered brown dots, contributing to the diagnosis of superficial cancers (Figure 14). Moreover, close BLI examinations using transnasal endoscopy enable the physician to obtain a mucosal diagnosis, even without magnification.

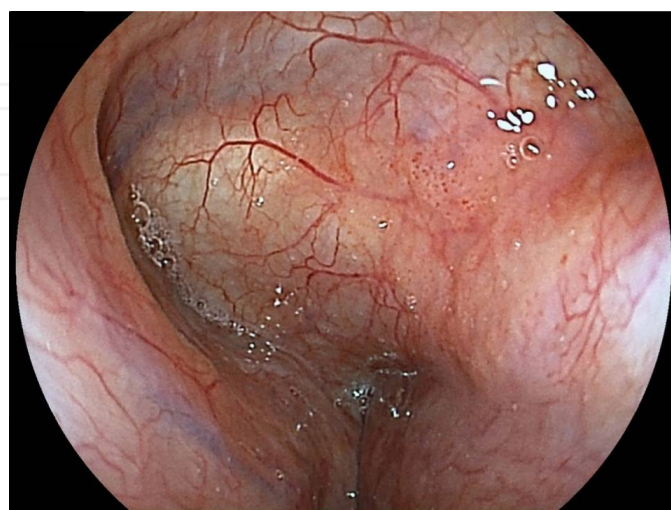


Figure 13. The white light image showed a 0-II b lesion of the right piriform sinus.

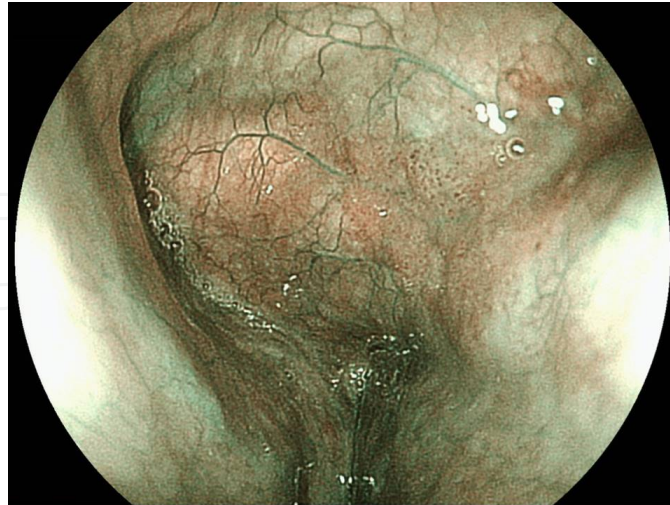


Figure 14. The close BLI image showed brown dots in the 0-II b lesion.

The modified Valsalva maneuver is also useful for detecting proximal invasion of the cervical esophageal cancer. This maneuver helps the physician to determine whether to preserve the patient's voice during surgery. On conventional screening, endoscopic images of hypopharyngeal cancer are often observed, however the distal part of the tumor is not visualized (Figure 15). A BLI endoscopic image obtained during the modified Valsalva maneuver using transnasal ESD is shown in Figure 16. The whole image of the tumor was able to observe (Figure 17). The entire tumor was observed, as indicated in Figure 17: the advanced cervical esophageal cancer had invaded the hypopharynx.

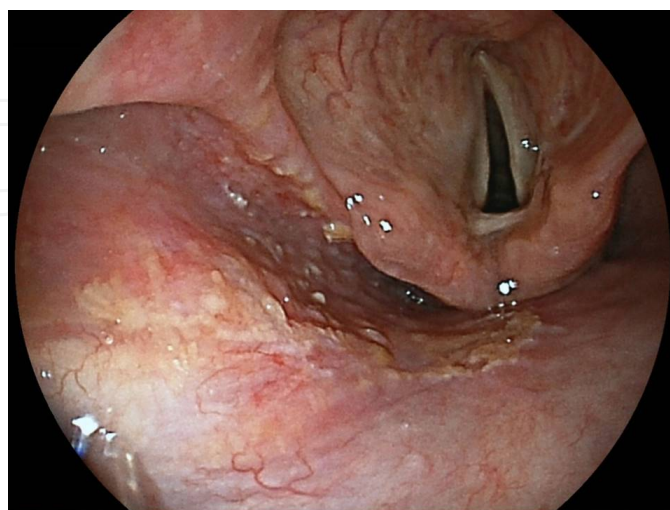


Figure 15. A reddish and irregular mucosa was shown in the hypopharynx. The distal part is not visualized.

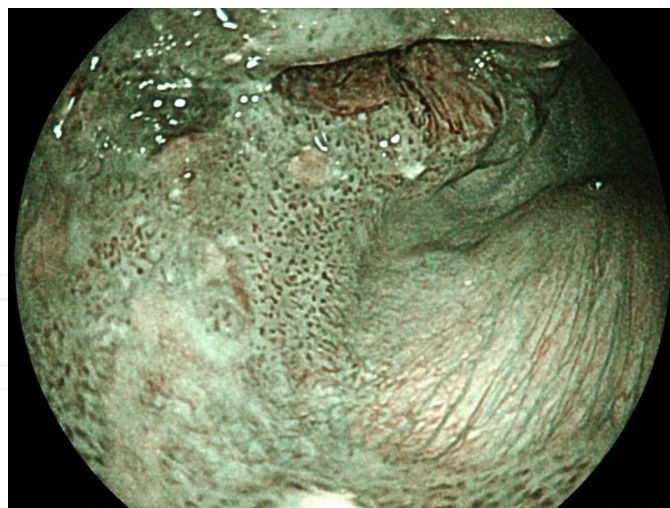


Figure 16. Advanced cancer was observed at the pharyngoesophageal junction using BLI during the trumpet maneuver.

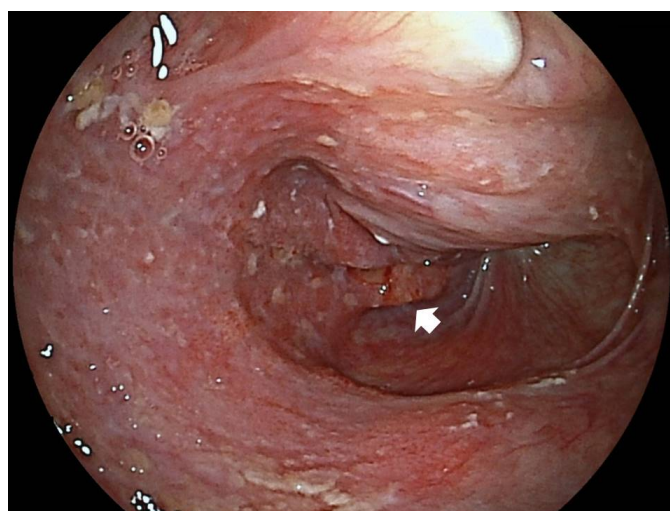


Figure 17. The advanced cervical esophageal cancer had invaded the hypopharynx (arrows).

6. Further research

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 oropharyngeal and hypopharyngeal cancers. The development of transnasal endoscopy with the BLI system now enables the wider observation and can be used to obtain adequate information for diagnosing early cancers without magnification. The modified Valsalva maneuver and intra-oropharyngeal U-turn method using transnasal endoscopy are not popular in Japan as of yet, however these techniques are very easy to perform, and we expect that this method will become a

standard procedure for observing the pharynx and orifice of the esophagus in the near future. Nevertheless, further studies, including randomized, prospective, multi-institutional joint trials comparing conventional endoscopy with the NBI system or transnasal endoscopy with the BLI system are required.

Transnasal endoscope technology is continually improving. From the viewpoint of early detection of pharyngeal cancer, we hope that transnasal endoscopy will become more widely adopted.

7. Conclusion

The significant progress achieved in the field of transnasal endoscopy rapidly within the last few years has improved the ability to observe the blind area typically noted during conventional screening. Therefore, transnasal endoscopy is expected to become a standard tool for screening of the upper gastrointestinal tract in the near future.

Author details

Kenro Kawada^{1*}, Tatsuyuki Kawano¹, Taro Sugimoto², Toshihiro Matsui¹, Masafumi Okuda¹, Taichi Ogo¹, Yuuichiro Kume¹, Yutaka Nakajima¹, Katsumasa Saito¹, Naoto Fujiwara¹, Tairo Ryotokuji¹, Yutaka Miyawaki¹, Yutaka Tokairin¹, Yasuaki Nakajima¹, Kagami Nagai¹ and Takashi Ito³

*Address all correspondence to: kawada.srg1@tmd.ac.jp

1 Department of Esophageal and General Surgery, Tokyo Medical and Dental University, Tokyo, Japan

2 Department of Otorhinolaryngology, Tokyo Medical and Dental University, Tokyo, Japan

3 Department of Human Pathology, Tokyo Medical and Dental University, Tokyo, Japan

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