APPLICATION OF UNSEDATED TRANSNASAL ESOPHAGOGASTRODUODENOSCOPY IN THE DIAGNOSIS OF HYPOPHARYNGEAL CANCER

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Abstract: Background. This study evaluates the efficacy of unsedated transnasal esophagogastroduodenoscopy (EGD) in the diagnosis of hypopharyngeal cancer and screening of esophageal lesions.

Methods. Twenty-seven patients with newly diagnosed hypopharyngeal cancer were evaluated by transnasal EGD without conscious sedation.

Results. Twenty-two hypopharyngeal cancers arose from the pyriform sinus, and the other 5 tumors were from the posterior hypopharyngeal wall. Seventeen tumors were classified as T3-T4. Twenty-four hypopharyngeal tumors were pathologically proved malignancy by this technique. Regarding simultaneous esophageal lesions, esophageal dysplasia was noted in 4 patients and esophageal cancer occurred in 6 patients. The procedures were performed without difficulty except in 1 patient with huge posterior wall tumor. The mean procedure time was 22 minutes. All patients tolerated the procedure well, without significant bleeding or respiratory distress during examination.

Conclusion. Unsedated transnasal EGD is a safe, tolerable, and accurate endoscopic technique for diagnosis of hypopharyngeal cancer and screening of simultaneous esophageal cancer.

Keywords: hypopharyngeal cancer; transnasal esophagogastroduodenoscopy; esophageal cancer; double cancer; field cancerization

Hypopharyngeal cancer is 1 of the most common head and neck cancers, with the poorest prognoses among others. Because hypopharyngeal tumors are deeply seated in the throat and partially obscured, it is difficult to diagnose and evaluate hypopharyngeal cancer under local anesthesia. Currently, rigid laryngoscopy under general
anesthesia is commonly used in clinical practice for biopsy of hypopharyngeal tumors and evaluation of the tumor extent for treatment options, especially for surgical purposes. However, in many countries, patients with hypopharyngeal cancer usually have trismus and stiff neck due to betel nut chewing. Thus, it is sometimes difficult to diagnose hypopharyngeal cancer even using a rigid laryngoscope under general anesthesia. Additionally, some hypopharyngeal tumors are so locally advanced that intubation for general anesthesia is difficult and risky for airway obstruction following general anesthesia. Tracheotomy is sometimes needed in this condition, making further management of hypopharyngeal cancer more complicated. Furthermore, second primary cancers, especially esophageal cancer, are not uncommon in patients with hypopharyngeal cancer with the incidence of 10% to 20%, which may partly account for the poor prognosis despite adequate control of primary tumors. Rigid esophagoscopy under general anesthesia concurrent with laryngoscopy is 1 of the diagnostic tools used for screening of simultaneous esophageal cancer. However, this procedure is always difficult in patients with advanced hypopharyngeal cancer and may miss small esophageal lesions. Therefore, barium esophagogram or flexible gastroscopy is always performed to exclude simultaneous esophageal lesions.

Unsedated transnasal esophagoscopy or esophagogastroduodenoscopy (EGD) is a new endoscopic technology that allows comprehensive examination of the upper aerodigestive tract from the nasal cavity to the stomach. Because of its small caliber, ability in air insufflation, and the inherence of instrument channel for suction and biopsy, unsedated transnasal esophagoscopy or EGD may overcome the aforementioned difficulties in diagnosis of hypopharyngeal cancer and may be a promising standard diagnostic tool for hypopharyngeal cancer. Reviewing previous studies on the application of unsedated transnasal esophagoscopy or EGD in otolaryngology; however, most investigations have focused on benign diseases, such as globus pharyngius, reflux esophagitis, esophageal foreign body, or placement of the tracheoesophageal puncture. Only a limited number of studies have limited experience about the role of unsedated transnasal esophagoscopy or EGD in head and neck oncology. In this article, we provide a detailed report on the efficacy and safety of unsedated transnasal EGD in the diagnosis of hypopharyngeal cancer and screening of simultaneous esophageal lesions.

**PATIENTS AND METHODS**

All patients with suspicious hypopharyngeal cancer, either newly diagnosed cases without previous head and neck cancer, or metachronous second primary cancers to previously treated other head and neck cancer, were enrolled in this prospective study, which was reviewed and approved by the institutional review board at National Taiwan University Hospital. The exclusion criteria were allergy to iodine and prior esophageal resection. The TNM status of each tumor was classified according to the 2002 criteria of the American Joint Committee on Cancer.

**Technique of Transnasal Ultrathin Endoscopy.** After an overnight fast, patients received topical anesthesia with cotton pledges soaked in a mixture of 0.1% epinephrine/1% cocaine solution (1:1) placed in their nasal cavities for 10 minutes. Several sprays of 10% xylocaine were administered to the oropharynx. None of the patients received conscious sedation. Next, patients were placed in the left lateral decubitus position for endoscopic examination. An ultrathin endoscope (GIF-XP260N; Olympus Optical, Tokyo, Japan) with 4-way angulation capability, a distal end of 5 mm in diameter, an insertion tube of 5.5 mm, and a suction channel of 2 mm, was lubricated and then passed into the nasal cavity either along the inferior meatus or between the middle and inferior turbinates. The laryngeal structures including the supraglottis and vocal fold movements and the hypopharyngeal structures including bilateral pyriform sinus and their apex, post-cricoid area, and posterior hypopharyngeal wall were all observed. When a tumor was present, the tumor extent was evaluated for further treatment plan and multiple biopsies were obtained through the instrument channel of the endoscope at the end of endoscopic examination. After evaluation of the hypopharyngeal lesion, the endoscope was passed into the esophagus to examine the mucosa of the entire esophagus for possible simultaneous esophageal lesions, using a combination of air insufflation and irrigation. The detection of esophageal lesions involved a sequential approach with conventional white light, narrow-band imaging (NBI system; Olympus Medical Systems, Tokyo, Japan), and Lugol chromoendoscopy, which has been previously reported in detail. All suspicious lesions in the esophagus were biopsied for histological confirmation.
RESULTS

Between May 2007 and January 2008, a total of 27 patients with newly diagnosed hypopharyngeal cancer were enrolled in this study (Table 1). Among them, 20 patients were classified as having fresh hypopharyngeal cancer without previous primary head and neck cancer. The remaining 7 patients had various types of other primary head and neck cancers, with complete remission ranging from 1 to 9 years prior to hypopharyngeal cancer diagnosis. These previous head and neck cancers included tonsillar cancer in 2 patients, nasopharyngeal carcinoma in 1 patient, epiglottic cancer in 1 patient, soft palate cancer in 1 patient, tongue base cancer in 1 patient, and tongue cancer in 1 patient. All of these 7 patients had been successfully treated with primary chemoradiation or surgery plus postoperative chemoradiation.

Twenty-two tumors were identified in the pyriform sinus and 5 tumors arose from the posterior hypopharyngeal wall. Ten tumors were locally early lesions (T1-T2) and the other 17 tumors were locally advanced lesions (T3-T4). All hypopharyngeal tumors were accurately evaluated by endoscopic examinations and verified by surgical findings or other preoperative images, except in 3 patients in whom the apex involvement was difficult to observe due to the locally too extensive tumors. Pathological examination proved malignancy in 24 hypopharyngeal tumors. Three biopsy examinations failed to obtain an adequate tissue sample to confirm the pathological diagnosis of malignancy and only yielded the diagnosis of squamous hyperplasia, hematoma, and ulcer. These 3 tumors included small ulcerative flat lesions on the posterior hypopharyngeal wall in 2 patients and a hypopharyngeal tumor hindered in the pyriform sinus near the apex with only smooth bulging mucosal surface exposed in 1 patient. All 3 lesions were then proved to be squamous cell carcinoma by subsequent rigid laryngoscopy under general anesthesia. Regarding the examination of the esophagus, 10 patients had simultaneous esophageal lesions, the pathological examinations of which revealed dysplasia in 4 patients (14.8%) and squamous cell carcinoma in 6 patients (22.2%). Three of these 10 patients with simultaneous esophageal lesions were the patients with second primary hypopharyngeal cancer (42.8%) and the other 7 patients were the patients with fresh hypopharyngeal cancer (35%). Of these 6 esophageal cancers, 2 were located in the cervical esophagus, 3 were in the mid-esophagus, and 1 was in the lower third esophagus. According to the results of this examination, patients with hypopharyngeal cancer without simultaneous esophageal cancer received curative treatment following the protocol of this hospital and the patient’s will. Of the 6 patients with simultaneous hypopharyngeal and esophageal cancers, 2 patients received radical surgery plus postoperative chemoradiation, 3 patients received induction chemotherapy plus surgery/chemoradiation, and 1 patient with epiglottic cancer treated with radiation 9 years ago received photodynamic therapy with Photofrin for his small hypopharyngeal cancer in the posterior wall and esophageal cancer in the mid-esophagus (both T1).

The procedures were performed without difficulty except in 1 patient with locally advanced posterior wall hypopharyngeal cancer. In this patient, the endoscope was unable to pass through
the hypopharyngeal tumor into the esophagus for complete evaluation. The entire procedure time including evaluation of the hypopharynx and esophagus and biopsies of the multiple sites ranged from 10 to 52 minutes, with a mean duration of 22 minutes. All patients tolerated the procedure well, and none converted to general anesthesia. No significant bleeding from the biopsy sites or airway obstruction was noted during the examination. After examination, no obvious discomfort was noted, except in 1 patient in whom we observed mild epistaxis, which spontaneously stopped within minutes without specific treatment, and in another patient who complained of mild chest discomfort, which may be related to Lugol’s examination of the esophageal lesion, and was quickly relieved by mild analgesics.

DISCUSSION

This study indicates that unsedated transnasal EGD is feasible and allows the otolaryngologists to obtain biopsy specimens of hypopharyngeal cancers, to evaluate the tumor extent, and to screen for the presence of simultaneous esophageal lesions in a single session. Even for patients with locally advanced hypopharyngeal cancers with T4 classification, unsedated transnasal EGD was safe and prevented potential airway obstruction following conventional laryngoscopy under general anesthesia in at least 3 patients with bulky hypopharyngeal tumors. Conventional unsedated transoral esophagoscopy or EGD may be another option for the diagnosis of nontrismus hypopharyngeal cancers, but unsedated transnasal EGD is more tolerable for comprehensive evaluation of hypopharyngeal cancer from the hypopharynx to the stomach even when the examination time approached 1 hour in 1 case. Conventional transoral esophagoscopy or EGD is much less tolerable for such a long duration without conscious sedation. For those who had trismus or had undergone treatment for previous head and neck cancer, unsedated transnasal EGD seems to be the best tool compared to other diagnostic modalities. For patients with hypertrophic turbinates or marked deviation of the nasal septum, our study demonstrated that transnasal EGD was still successfully performed through the nasal meatus as long as adequate mucosal shrinking and anesthesia were applied.

Because the hypopharyngeal tumor is proximal to the airway opening, some clinicians may have concerns regarding bleeding or suffocation, and may hesitate to obtain biopsies of the hypopharyngeal tumor during endoscopic examination without airway security. In this series, bleeding after biopsy was usually minimal, and all patients tolerated it well without respiratory distress during and after endoscopic examination. In fact, most of the patients in this series had no significant complications. Only 1 patient had mild epistaxis and the other had mild chest discomfort.

Although biopsy forceps of the transnasal EGD are smaller, accurate pathological diagnosis of hypopharyngeal cancer were made in most cases of this series. Certainly, more practice and sufficient time for a learning curve is needed before the procedure can be performed to obtain enough tissue from a transnasal EGD biopsy. From the experience of this series, small ulcerative flat lesions, especially on the posterior hypopharyngeal wall, and small tumors hindered in the pyriform sinus near the apex with only smooth bulging mucosal surface exposed were considered difficult to obtain adequate tissue for confirmatory diagnosis. However, even for such kinds of lesions, transnasal EGD without conscious sedation may still be the first choice for diagnosis of hypopharyngeal cancer. Conventional rigid laryngoscopy under general anesthesia may be reserved for those who failed to be pathologically diagnosed by transnasal EGD. Except for too locally advanced tumors, evaluation of the tumor extent by transnasal EGD was generally well correlated with surgical findings. From an endoscopic view, examiners can confirm tumor involvement of medial, lateral, or posterior wall of the pyriform sinus and of intralaryngeal structures, which are sometimes difficult to distinguish by imaging studies alone. The vocal fold function is clearly demonstrated by transnasal EGD, which cannot be assessed by traditional rigid laryngoscopy under general anesthesia or static imaging studies. The upper esophageal sphincter and pyriform sinus apex can be evaluated by transnasal EGD, especially when the endoscope is pulled out from the esophagus.

Because of field cancerization caused by betel nuts, alcohol, and smoking, esophageal cancer is not uncommon as a second primary cancer in patients with hypopharyngeal cancer. Undetected simultaneous esophageal cancer will worsen the prognoses of patients, even though their hypopharyngeal cancers are successfully treated. Therefore, some diagnostic strategies regarding the evaluation of hypopharyngeal cancer are suggested in clinical practice, such as selective screening in patients with significant...
dysphagia and routine screening of esophageal cancer through barium esophagogram or gastroscopy.\textsuperscript{19,20} In this study, unsedated transnasal EGD was able to detect and pathologically diagnose simultaneous invasive esophageal cancer in 6 patients (22.2\%), 2 of whom had small T1 lesions that had no associated symptoms and may be missed by barium esophagogram. The treatment plans of these 6 patients were all changed for these simultaneous cancers. Further, esophageal dysplasia lesions were noted in another 4 patients (14.8\%) with adjunct of NBI and Lugol’s staining. These 4 patients had a theoretically higher risk for developing second esophageal cancer and were the candidates for close endoscopic surveillance after treatment of hypopharyngeal cancer.\textsuperscript{18} Taken together, about one third of hypopharyngeal cancers were determined to have precancerous or cancerous lesions in the esophagus in this series, indicating that a routine examination of the entire esophagus in patients with hypopharyngeal cancer is necessary. Unsedated transnasal EGD is a convenient and feasible tool for completing this work.

**CONCLUSION**

Unsedated transnasal EGD is a safe, tolerable, and accurate endoscopic technique for pathological diagnosis of hypopharyngeal cancer and screening of simultaneous esophageal cancer during a single session. It is particularly useful in patients with locally advanced tumor, trismus, stiff neck, or previously treated primary head and neck cancer.

**REFERENCES**