Chapter 47
NBI® assessment of premalignant and malignant laryngeal lesions

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Abstract

The methods of “biological” endoscopy are intensively developing in recent years. The images obtained with these methods display more details of mucosa structure in order to make the clinical diagnosis as most accurate and close to histopathology as possible. Such aim is particularly important in premalignant changes of the larynx mucosa. We present our experience in the assessment of the laryngeal lesions with one “biological” endoscopy method, Narrow Band Imaging (NBI®). Based on the assessment of the appearance of blood vessels within the lesion and in the surrounding mucosa of the larynx with NBI®, we can with high sensitivity determine the risk of high-grade dysplasia or invasive cancer. In addition, NBI® is a useful and more accurate tool than white light (WL) endoscopy in the evaluation of the extent of the laryngeal mucosa, thus providing more precise staging. Also in patients after radiotherapy and post-radiation changes of laryngeal mucosa, the NBI® method appears very promising in the diagnosis of cancer recurrence.

Keywords: laryngeal lesions, dysplasia, leukoplakia, non-invasive laryngeal carcinoma, invasive laryngeal carcinoma, NBI®, LVS

Introduction

Laryngologists face many difficult cases, but those that are suspect for premalignant or malignant lesions of laryngeal mucosa are among the most challenging. Diagnosis based on indirect laryngoscopy that reveals leukoplakia, chronic laryngitis, or thickening of vocal fold (VF) mucosa may eventually represent quite a wide range of histopathological diagnosis ranging from hypertrophy and parakeratosis through the three grades of dysplasia up to noninvasive and/or invasive carcinoma.

It is well recognized that treatment methods are entirely different for the benign VF conditions compared to malignant conditions. Hence, enhancement of visual diagnostics is desired. NBI® serves such a purpose. NBI® was only recently introduced in laryngology to achieve better visualization of mucosa and submucosal vessels and thereby to identify neoangiogenesis accompanying malignant transformations. NBI® derived laryngeal lesions were first classified by Ni et al. in 2011 [1] and this classification enables a more detailed endoscopic differentiation of laryngeal lesions that is unobtainable with laryngovideostroboscopy (LVS).

Results

We have now experienced three months of NBI® usage in our clinic to study laryngeal lesions. The equipment is the Olympus Visera Elite OTV-S190 system. Using NBI® allowed us to estimate the usefulness of this method in the assessment of the laryngeal pathol-
ogy before elective performing MDL procedures in patients presenting with malignant laryngeal lesions. Surprisingly, we also observed that NBI® can be quite helpful in assessment of patients with non-malignant mucosal changes (i.e., in the case of leukoplakia). On WL endoscopy we see in these cases only the white plaque. On NBI® we can now classify (Ni classification) these images as Type III. In some cases we can see that the white layer is quite thin and the vessels beneath are regular including the vessels surrounding the plaque. This very descriptive diagnosis is nonetheless helpful in making further clinical decisions.

Experiencing rather a quite large group of similar cases in our practice, the NBI® has enabled us to refrain from the biopsy and to follow-up these cases longitudinally. Unfortunately, this thick white plaque still presents “unreadable” conditions. However, in these cases we try to intensively examine the vessels surrounding the “leukoplakia” and based on such observations we can stratify the risk of dysplasia in the mucosa. Using this approach in 10 patients presenting with thick white plaque, we identified (using NBI®) two cases with irregular shape and oblique or perpendicular arrangement of blood vessels in the vocal fold mucosa, which on histopathological exams showed to be mild and moderate dysplasia. The rest of the eight cases represented hyperkeratosis. We trust that such observations can be interesting, hence further detailed analysis is warranted.

Figure 1A shows a thin layer of leukoplakia with WL endoscopy. On the right VF, the plaque is translucent, allowing imaging of the blood vessels of mucosa. Although these blood vessels are extended, NBI® (Figure 1B) renders them as regular.

Figure 2 shows a thick layer of leukoplakia (Figure 2A is from LVS examination). This is classified on NBI® as Type III according to Ni (Figure 2B). Magnified NBI® image of the area marked with dotted surrounding in Figure 2B shows the plaque (marked with yellow arrow in Figure 2C) displaying irregular pattern of vessels in the mucosa.

Figure 1. A thin layer of leukoplakia illuminated with WL endoscopy (A) and NBI® (B).

Figure 2. A thick layer of leukoplakia from LVS examination (A) and NBI® (B); C) magnified section of yellow dotted area in (B) displays irregular pattern of vessels.
We agree that the most important and useful aspect of NBI® is surely connected with its very high sensitivity and specificity in differentiation of benign hypertrophic lesions from malignancies. Out of 40 patients with laryngeal lesions that were examined with NBI® before microsurgery, we were able to identify 18 as vascular patterns (Ni classification) representing Types Va, Vb, or Vc; 16 of them confirmed on histopathology as non-invasive or invasive planoepithelial carcinoma. The two cases of Va were high grade dysplasia in papillomatosis.

Figure 3A shows the right VF tumor on LVS examination. The same tumor shows on NBI® with visible dilated vessels suggesting Type II (Figure 3B). However magnified NBI® of the area marked with dotted line revealed brown, scattered dots within the lesion (yellow arrow), suggestive of Type Va (Figure 3C).

Figure 4A represents LVS examination of larynx with right VF tumor and leukoplakia on left VF and left ventricular fold. The same larynx seen under NBI® illumination shows visible brown dots within the tumor on right VF. It was classified as Type Va (Figure 4B).

Another practical aspect of NBI® is that during the direct laryngoscopy and biopsy taking, we have often been unsure of what we are expecting to discover and at what location the biopsy should be taken to get the true histopathological result. That is why multiple biopsies from few places are taken. Performing NBI® before the biopsy procedure enhances decision making with regards to biopsy location.
Figure 5A represents the LVS revealing the subglottic tumor and synechia of anterior commissure. The NBI® visualized the tissue of anterior commissure with pathological vessels of Type Vb (Figure 5B).

![Figure 5. Subglottic tumor and synechia of anterior commissure from LVS examination (A) and NBI® (B).](image)

The additional advantage of NBI® that we found is a more precise staging of tumor size. We experienced few patients that we diagnose as T1 glottis cancer on LVS and prepared them for cordectomy. Just after performing NBI®, we were obliged to upgrade the staging to T2 and modify the treatment approach to radiotherapy. In these cases, the NBI® has allowed us to avoid exposing the patient to general anaesthesia and unnecessary tissue loss.

Figures 6A shows endoscopy with WL displaying right VF tumor. The NBI® revealed the tumor of right VF classified as Type Vc. However, the pathological vessel pattern was localized on both the right ventricular fold (single filled star) and in the subglottic area (double empty stars).

![Figure 6. Right VF tumor illuminated with WL endoscopy (A) and NBI® (B). NBI® shows pathological vessel patterns in the right ventricular fold as well as in the subglottic area.](image)

With regards to the diagnosis of laryngeal cancer reoccurrence in patients after radiotherapy, we all can agree that these cases are usually very problematic both for LVS assessment or with CT imaging due to inflammation and edema caused by radiation exposure. Zabrodsky et al. [7] informs us about very high sensitivity (100%) and specificity (92%) of LVS combined with magnifying NBI® endoscopy. Our experience so far include four patients with history of radiation due to T2 laryngeal cancer and admitted with sus-
picion of recurrence. On NBI® examination (prior to direct laryngoscopy under general anesthesia), we found Type II in two patients, excluding the recurrence and Va and Vb in the other two with actual recurrence, which was confirmed later with histopathology results.

Figure 7A shows an LVS image of larynx after radiotherapy due to laryngeal cancer with reoccurrence in the anterior commissure. The NBI® confirms pathological vessels in the tissue of anterior commissure (Figure 7B). Moreover, magnified NBI® of the area marked with the yellow dotted line revealed pathological vessels both on ventricular folds and on laryngeal surface of the epiglottis (Figure 7C).

![Figure 7](image)

**Figure 7.** Laryngeal cancer reoccurrence after radiotherapy illuminated with WL endoscopy (A) and NBI® (B). C) magnified section displays pathological vessels on ventricular folds as well as on laryngeal surface of the epiglottis.

Figure 8A shows WL endoscopy of irradiated larynx. The assessment was difficult due to accompanying inflammation. However, NBI® revealed pathological vessel pattern on right VF as Type Vb (Figure 8B).

![Figure 8](image)

**Figure 8.** Irradiated larynx illuminated with WL (A) and NBI® (B).

**Reflux on WL and on NBI®**

Finally, we include our preliminary NBI® observations in patients with symptoms of gastro-esophageal reflux. In this group we observed in the posterior commissure and in the post-cricoid area the pathological vessel pattern of Type IV. In this area we usually find erythema and hyperplastic changes using WL, whereas on NBI® we can see the dilatation and proliferation of epithelial micro-vessels caused by chronic inflammation condition. It is interesting to correlate the NBI® classification with the severity of reflux laryngitis.

Figure 9A shows an LVS image of reflux laryngitis with VF edema and hyperplastic changes in the posterior commissure. The NBI® view of the same larynx is shown in Figure 9B. The magnified NBI® of the posterior commissure of this larynx reveals vessel pattern of Type IV (Figure 9C).
Summary and conclusions

We have documented here the advantages of using NBI® in examining laryngeal lesions and although “visual biopsy” is still in its infancy, we are of the opinion that NBI® is a powerful tool to differentiate among the malignant and non-malignant lesions.

References