The Narrow Band Imaging as an essential complement to White Light Endoscopy in Recurrent Respiratory Papillomatosis diagnostics and follow-up process

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ABSTRACT:
The aim of the study is to discuss the role of NBI imaging in upper respiratory papillomatosis (RRP). In the available literature on the subject, as of 2009, there have been 117 publications on NBI imaging focusing on the diagnosis of the upper respiratory and digestive tract, especially the larynx. They discuss the following diagnostic and therapeutic problems: identifying an abnormal vascular pattern within the mucosa, differentiating benign and malignant lesions, assessing the nature of lesions under the leukoplakia plaque, pre-operative definition of laryngeal cancer margins, supporting laser procedures to obtain safe margins, postoperative monitoring after cancer treatment, detecting second simultaneous and metachronic neoplasms and primary tumors in the case of metastases from an unknown primary site. Few reports have been devoted to the assessment of the extent and recurrence of RRP. Due to its recurrent nature, this pathology deserves special attention as it requires multiple inspections and manipulation within the larynx. It also applies to the pediatric population, where there should be no margin for underestimating or overestimating changes, because any suspicion of recurrence results in subsequent general anesthesia. Hence the attempt to define an unambiguous picture of RRP recurrence and the criteria for referring for subsequent surgical treatment.

KEYWORDS:
endoscopy, larynx, Narrow Band Imaging, recurrent respiratory papillomatosis

ABBREVIATIONS
CAD – Computer-Aided Diagnosis
ELS – European Laryngological Society
NBI – Narrow Band Imaging
RRP – recurrent respiratory papillomatosis
WL – white light
WLE – white light endoscopy

INTRODUCTION
Narrow Band Imaging (NBI) is an endoscopic optical technique working with a filtered light that enhances visualization of mucosal and submucosal vasculature. NBI improves the mucosal surface assessment and is positively correlated with angiogenesis indexes in immunohistological evaluation [1]. Due to its properties, it can allow a clear view of suspected malignant or precancerous lesions earlier than conventional white light (WL) endoscopy and correlates strongly with histopathologic results [2].

NBI serves as a useful adjunct to WL endoscopy in the diagnosis of numerous laryngeal and hypopharyngeal lesions since the first decade of the XXI century [3–4]. In the available literature on the subject, as of 2009, there have been 117 publications on NBI imaging focusing on the diagnosis of the upper respiratory and digestive tract, especially the larynx. They discuss the following diagnostic and therapeutic problems:

• identifying an abnormal vascular pattern within the mucosa [5–7],
• differentiating benign and malignant lesions [8–16],
• description of the usefulness of new ELS classification [17], which enables to effectively and safely differentiate malignant from benign disease [18–20],
• assessing the nature of lesions under the leukoplakia plaque [5, 9, 21, 22] and avoiding the umbrella effect [23],
• pre-operative definition of laryngeal cancer extent [24, 25],
• supporting laser procedures to obtain intraoperative safe margins [13, 26–28, 29, 30],
• postoperative monitoring after cancer treatment [31, 32].

NBI combined with laryngovideostroboscopy or stroboscopy differentiate low- and high-risk malignancy lesions of vocal fold leukoplakia, supporting comprehensive clinical evaluation assessing morphology, vibratory function, and vascular pattern [33,
NBI creates the opportunity for tissue sampling of suspicious recurrence in head and neck cancer patients with difficult airways [35], precise detecting of second primaries, simultaneous and metachronic neoplasms [36] and primary tumor foci in the case of metastases from an unknown primary site [3].

Few reports concerning NBI imaging are devoted to the assessment of the primary extent and recurrence of RRP [37–40]. Due to its recurrent nature, this pathology deserves special attention as it requires multiple inspections and manipulation within the larynx. It also applies to the pediatric population, where there should be no margin for underestimating or overestimating mucosal changes, because any suspicion of recurrence results in subsequent general anesthesia. Hence the aim of the study is to discuss the role of NBI imaging in upper respiratory papillomatosis and to make an attempt to define an unambiguous picture of RRP onset or recurrence at follow-up and the criteria for referring to subsequent surgical treatment.

RESULTS

The characteristic feature of RRP is wart-like lesions covering the respiratory epithelium. The goal of the treatment is a total surgical removal of the papillomatous lesions in order to reduce the number of relapses and preservation of healthy mucosa and vocal fold structure. Therefore, a good visualization method of papillomas is crucial during surgery and follow-up (Fig. 1., 2.).

The case report of Imaizumi in 2012 presented the NBI system in two patients with RRP and showed that the border between the normal mucosa and the papillomas could be clearly identified, allowing precise resection and RRP eradication without further recurrence.

Simultaneously, in 2012 the first prospective study on 14 RRP patients was published by Tjon Pian Gi et al. Eighty-six excisional biopsies were taken in 24 microlaryngoscopies after a systematic inspection of the larynx during microlaryngoscopy using conventional white light immediately followed by inspection with NBI; the sensitivity increased from 80% with WL up to 97% with WL + NBI, whereas the specificity remained poor, i.e. 32% and 28%, respectively.

The usefulness of NBI in the assessment of laryngeal papillomatosis in a set of 10 patients was showed by Ochsner et al. in 2015. Ten pairs of pictures were collected and sent to multiple fellowship-trained laryngologists, along with a questionnaire designed to evaluate visualization with NBI versus WL; the study suggested that NBI better defined the borders of diseased tissue and may provide some benefit in the visualization and treatment of LP in an awake patient.

One of the largest groups of RRP patients was presented by Jackowska et al. in 2018. The study was carried with conventional white light (WL) and NBI (CV-260SL processor and CLV-260SL light source, Olympus Optical Co. Ltd, Tokyo, Japan) in 36 patients assessed by means of the Dikkers scale and Derkay scoring system; it was proved, that NBI as an additional tool during microlaryngoscopy, can improve the detection of papillomatous lesions and increase the accuracy of the grade of RRP advancement.

DISCUSSION

Benign lesions of the larynx are frequently characterized by longitudinal vessels or an absence of vessels in the area of the lesion, thus the combination of white light and NBI endoscopy enables a better detection compared to WL endoscopy alone. The use of NBI for the detection of benign lesions of the larynx (vocal fold cyst, polyp, Reinke’s edema, granuloma) was described [41–43]. Capillary vessels in papillomas absorb the narrow band light and show typical brown or increased intraepithelial papillary capillary pattern within a lobular, shimmering, pale, wart-like mass. By Arens, the papilloma is associated with loops with wide-angled turning points embedded in a warty structure in contrast to the cancer where there are loops with narrow-angled turning points [17]. The primary suspicion for RRP during office laryngoscopy is based on lesion appearance, but the findings in NBI vascular pattern are scarce. The usefulness of refining the method may be
of particular importance in planning the office-based procedures [44] to guide classic cold steel or laser procedures in general anesthesia and to precisely locate the points of sublesional injection in topical drug administration.

**RRP as a rare disease**

RRP is a much rarer pathology than precancerous conditions or larynx cancer, so they have not been given rating scales like in cancer or leukoplakia. Sensitivity, specificity, positive predictive value, negative predictive value, accuracy and likelihood of endoscopic examination comparing WLE alone and WLE + NBI in RRP are lacking. Most of the experience regarding the value of using the NBI method is also drawn from pre-cancerous processes and mucosal cancers. On the other hand, the philosophy of demeanour in the case of RRP is diametrically different than in cancer. In cancer, the principle is to estimate the lesion and to achieve the widest possible excision with a safe margin, while in papillomas the priority is not to overestimate the lesion, leaving the normal epithelium and deeper layers of the vocal fold intact.

**NBI method limitations**

Observers tend to estimate vocal fold lesions to be larger and more frequently suspect malignancy while assessing NBI images. Compared to WL, NBI demonstrates increased sensitivity and decreased specificity for detection of malignancy [8]. This would not be beneficial for the treatment of RRP. On the other hand, NBI represents a reliable technology in challenging situations, especially in the context of post-radiotherapy or post-surgical mucosal changes showing a higher negative predictive value [32]. Based on other scientific group experience, NBI could reduce the number of unnecessary biopsies related to increased microvascular anomaly revelations, and, consequently, decrease hospital admissions [32], but simultaneously could help to identify early-stage lesions suitable for minimally invasive surgery. This philosophy can and should be applied for RRP diagnostics.

The next problem to solve is that the visual evaluation of vascular patterns in NBI images is challenging and highly depends on the clinicians’ experience [7]. The learning curve for endoscopic evaluation of vocal folds’ lesions with NBI is long and a minimum of 65–70 sessions are required to reach a plateau phase of the learning process in the assessment of glottis lesions [45].

**New technological solutions**

Some groups aim to evaluate and compare the performance of a manual and an automatic approach for laryngeal lesion’s classification based on NBI images’ vascular patterns [2, 46, 47]. For the automatic classification, an algorithm based on characterizing the level of the vessel’s disorder in combination with supervised classifiers was presented and the automatic approach showed the potential to work as an assistant system in case of disagreements among clinicians and to reduce the manual approach’s misclassification issue [2]. NBI image classification served to test a novel approach for texture feature extraction, which is an essential part of a Computer-Aided Diagnosis (CAD) system. It is usually preceded by a pre-processing step and followed by image classification. Usually, a large number of features is needed to end up with the desired classification results.

This method, tested on the larynx provides more objective information for otolaryngologists regarding the stage of the laryngeal cancer. Thus, NBI images can be a part of the CAD system in combination with Geometrical Features for laryngeal cancer diagnosis, which represent a high number of patients’ pathology [47]. The translation for RRP pathology will be challenging because of the limited number of patients, but it is a chance to improve the diagnostics’ accuracy and has a potential future direction.

**REFERENCES**


