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구강 백반증 진단에 있어서 i-scan image-enhanced 내시경의 진단적 유용성

이영찬[1] · 은영규[1] · 박일석[2+]

[1]경희대학교 이비인후과학교실, [2]한림대학교 동탄성심병원 이비인후과학교실

The diagnostic value of i-scan image-enhanced endoscopy in the diagnosis of oral cavity leukoplakia

Young Chan Lee, MD, PhD[1], Young-Gyu Eun, MD, PhD[1], Il-Seok Park, MD, PhD[2+]

Department of Otolaryngology—Head and Neck Surgery, School of Medicine, Kyung Hee University, Seoul, Republic of Korea[1], Department of Otorhinolaryngology—Head and Neck Surgery, Hallym University College of Medicine, Dongtan Sacred Heart Hospital, Hwaseong, Republic of Korea[2]

= Abstract =

Background/Objectives: The aim of this study was to investigate the diagnostic value of i-scan in the differential diagnosis of oral cavity leukoplakia based on visualization of abnormal vascular features.

Materials & Methods: Thirty- one patients with oral cavity leukoplakia were enrolled in the study. Images of their oral cavity obtained using conventional white light endoscopy and an i-scan-enhanced endoscopy (Pentax DEFINA EPK-3000 Video Processors, with Pentax VNLJ10) were reviewed. The microvascular features of the lesions and vascular changes were analyzed and the results were compared with the histopathologic diagnosis.

Results: Among the 31 oral cavity leukoplakia patients, 8 (25.8%) patients revealed hyperkeratosis, 10 (31.2%) low-grade dysplasia, 5 (16.2%) high-grade dysplasia and 8 (25.8%) invasive squamous cell carcinoma on histopathologic examination. Using i-scan-enhanced endoscopy, we could found abnormal vascular change with neoplastic neoangiogenesis in most high-grade dysplasia or invasive cancer in oral cavity. (high-grade dysplasia: 4/5 [80.0%], and invasive squamous cell carcinoma: 7/8 [87.5%]).

Conclusion: i-scan-enhanced endoscopy could be a useful optical technique for the diagnosis of oral cavity leukoplakia. Our results suggest that i-scan may be a promising diagnostic tool in the early detection of suspected oral mucosal lesion.

Key Words : Leukoplakia, Oral cavity, Carcinoma, i-scan

Introduction

Oral cavity leukoplakia is a relatively common disease of the oral mucosa.[1)] The pathologic results of clinically diagnosed oral cavity mucosal leukoplakia may be hyperplasia, mild or moderate dysplasia, severe dysplasia, or carcinoma. Furthermore, the degree of atypical hyperplasia is considered to be the most important prognostic factor for evaluating the risk of progression of malignant tumors in oral cavity leukoplakia.[2)] Therefore, Proper management of patients with oral cavity leukoplakia should always begin with accurate evaluation: visual examination followed by biopsy remains the most widely accepted first diagnostic step. However, conventional white light endoscopy (WLE) is not optimal in resolution and contrast, which is difficult

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+Corresponding author: Il-Seok Park, MD, PhD
Department of Otorhinolaryngology-Head and Neck Surgery, Endocrine-Thyroid Center Hallym University College of Medicine, Dongtan Sacred Heart Hospital 7, Keunjaebong-gil, Hwaseong-si, Gyeonggi-do 445-907
Tel: +82-31-8086-2670, Fax: +82-31-8086-2681
E-mail: ispark@hallym.or.kr

to distinguish between superficial mucosal cancer and precancerous lesions. The narrow band imaging (NBI) system (Olympus Medical Systems, Tokyo, Japan) is a noninvasive optical device that uses reflected light to visualize the superficial structure and enhance the appearance of the vasculature within the mucosal layer. Examination using NBI is greatly related to the morphology of microvessels, which include the intraepithelial papillary capillary loop (IPCL).[3] However, narrow band images are much darker than conventional WLE images.

i-scan technology is a newly developed image-enhanced endoscopy technology from PENTAX, Japan. i-scan images are as bright as conventional WLE images and do not need magnifying endoscopy to observe the demarcation of the lesion.[4] It has three modes of image enhancement: SE, surface enhancement (enhancement of the structure through recognition of the edges); CE, contrast enhancement (enhancement of depressed areas and differences in structure through colored presentation of low-density areas); and TE, tone enhancement (enhancement tailored to individual organs through modification of the combination of RGB components for each pixel). i-scan technology has been used in gastroenterology practice and has already been shown to improve the accuracy and diagnostic yield by identifying subtle abnormalities during endoscopy. Iacucci et al have found that i-scan improved the characterization of patchy atrophy of the villi in patients with celiac disease.[5] This helped in directing and targeting duodenal biopsies and improved the diagnostic yield. Graham and Banks found specialist upper gastrointestinal endoscopists using i-scan could detect dysplasia within a Barrett's segment with 75% sensitivity.[6]

We performed endoscopic visual examination with i-scan-enhanced endoscopy (Pentax DEFINA EPK-3000 Video Processors, with Pentax VNLJ10) in patients with oral cavity leukoplakia. The aim of this study was to evaluate the diagnostic value of i-scan in the differential diagnosis of oral cavity leukoplakia based on abnormal oral mucosal vascular features.

Material & methods

The study was approved by the institutional ethics committee and performed in accordance with the Declaration of Helsinki.

Subjects

Between March 2016 and September 2018, 31 oral cavity leukoplakia patients who underwent excisional biopsy for tissue biopsy confirmation were enrolled in this retrospective study. The selection criteria for the present study were as follows: 1) the presence of oral cavity leukoplakia, 2) no previous procedures (e.g., surgery, radiotherapy), and 3) preoperative endoscopy with WL and i-scan. The patients were examined using flexible endoscopy with WLE and i-scan (Pentax DEFINA EPK-3000 Video Processors, with Pentax VNLJ10). The patients with grossly exophytic tumor or ulcerative lesion were excluded. Age, sex, medical history, preoperative laryngoscopy on WL and i-scan, and pathologic histologic features were analyzed. The examinations were performed first with WL with a wide view to observe the whole lesion and the surrounding mucosa. Then, under i-scan, the same procedure was performed and the vascular features were analyzed in detail and recorded. i-scan consists of three different image algorithms: SE, TE, and CE. The three modes (SE, TE, and CE) are arranged in series; therefore, it is possible to apply two or more of these modes at one time. Switching of the level or mode of enhancement can be performed on a real-time basis, without any time lag, by pushing a scope button, enabling efficient endoscopic observation. i-scan 1, comprised of SE and CE, provides the user with a view that sharpens surface vessels and enhances surface texture of the mucosa. i-scan 2, comprised of SE, CE and TE mode c, provides the user with an image that increases the contrast between the mucosa and blood vessel. This increased contrast leads to improved visibility of blood vessels while also providing the same enhancements to the mucosal surface texture achieved in i-scan 1. i-scan 3 (SE, CE and tone enhancement mode g (TEg)) provides the user with increased visibility of blood vessels. The default setting for i-scan used in this study was SE 4+ and CE 3+. Image analysis of the microvascular features (regular and irregular) of the lesions and vascular change descriptions published by Arens et al. were followed; type I was defined as longitudinal vascular changes, enlarged and static vessels, meandering, tortuous, or dilated vessels, convoluted vessels, increased number of vessels or

branches of vessels “feeding” blood vessels; type II was defined as perpendicular vascular changes, real vessel loops with a wide-angled turning point embedded in a three-dimensional warty structure; type III was defined as enlarged and symmetric dot-like loops, abnormal IPCLs with narrow-angled turning points; and type IV was defined as abnormal worm-like vessels with spiral morphology and bizarre course.[7] They divided superficial vascular architecture in a quite simplistic and practical approach, through a dichotomous distinction between benign (longitudinal vessels) and premalignant or malignant (perpendicular vessels) lesions. The likelihood of malignancy is high in the order of type I to IV.

Excisional biopsy for pathologic confirm were performed after the patients provided written consent. The specimens from these patients were obtained from the archives of the Department of Pathology and reviewed by head and neck pathologists to verify the diagnosis and confirm the grade of dysplasia. Dysplasia of squamous epithelium

is a spectrum and graded as low, intermediate, or high, according to the World Health Organization (WHO) 2005 classification.[8]

Results

Thirty-one patients with oral leukoplakia were enrolled. The mean age was 68.2 years (range 48–82 years); 26 (83.8%) patients were male and 5 (16.2%) were female. Most oral leukoplakia were located in the tongue (20 (64.5%)). Among 31 patients, 8 (25.8%) patients had hyperkeratosis, 10 (31.2%) low-grade dysplasia, 5 (16.2%) high-grade dysplasia, and 8 (25.8%) invasive squamous cell carcinoma on histopathologic examination.(Table 1) Among the 8 patients with hyperkeratosis, longitudinal vascular patterns (type I) in the i-scan image were detected in 5 (71.4%) and type II perpendicular vascular changes in 2 (28.6%) patients. Among patients with low-grade dysplasia, 5/10 (50.0%) were identified as having a type I vascular pattern, 4/10 (40.0%) as having type II vascular change, and 1/10 (10.0%) as having type III abnormal IPCLs with narrow-angled turning points. Histologic features of high-grade dysplasia, or invasive squamous cell carcinoma were detected in 13/31 (41.9%) patients. i-scan identified neoplastic neoangiogenesis (type IV) in 1/5 (20.0%) and 5/8 (62.5%) patients with high-grade dysplasia and invasive squamous cell carcinoma, respectively. Abnormal IPCLs with narrow-angled turning points (type III) were found in 3/5 (60.0%) and 2/8 (25.0%) patients with high-grade dysplasia and invasive squamous cell carcinoma, respectively (Table 2).

Discussion

Leukoplakia is the most common premalignant or potentially malignant lesion of the oral mucosa. It seems preferable to use the term leukoplakia as a clinical term only. When a biopsy is taken, the term leukoplakia should be replaced by the diagnosis obtained histologically.[1] The different clinical types of leukoplakia, including homogeneous and nonhomogeneous types, are made based on surface color

Table 1. Demographic & clinical characteristics of enrolled patients

Variables	
Number of enrolled patients	31
Age	68.2 years (48-82 years)
Sex (Male/ Female)	
Male	26 (83.8%)
Female	5 (16.2%)
Pathology	
Oral cavity	
Hyperkeratosis	8 (25.8%)
Low-grade dysplasia	10 (31.2%)
High-grade dysplasia	5 (16.2%)
Invasive squamous cell carcinoma	8 (25.8%)

Table 2. Comparison of i-scan images for vascular feature and histopathologic findings.

Pathology	Microvascular feature type on i-scan			
	Type I	Type II	Type III	Type IV
Hyperkeratosis	5/8 (71.4%)	2/8 (28.6%)	0	0
Low-grade dysplasia	5/10 (50.0%)	4/10 (40.0%)	1/10 (10.0%)	0
High-grade dysplasia	0	1/5 (20.0%)	3/5 (60.0%)	1/5 (20.0%)
Invasive squamous cell carcinoma	0	1/8 (12.5%)	2/8 (25.0%)	5/8 (62.5%)

and morphological characteristics under broadband white light.[9] In addition to conventional WLE, many other "biologic endoscopy" methods (e.g., autofluorescence, contact endoscopy with vital tissue staining, and confocal endomicroscopy) have improved the rates of earlier detection of not only epithelial, but also vascular change in vocal cord.[10] Among them, narrow band imaging (NBI), which is an endoscopic imaging technique that emphasizes the mucosal microvasculature and identifies vascular alterations by placing narrow bandpass filters in front of a conventional white-light source to obtain tissue illumination at selected, narrow wavelength bands, is increasingly preferred and recommended for examining in laryngeal lesion.[11] i-scan is a newly developed image enhanced endoscopy technology from PENTAX. Although NBI is useful for detecting, diagnosing or identifying the demarcation line and predicting the histological characteristics of cancers with magnifying endoscopy, narrow band images are much darker than conventional white light images, particularly in large luminal diameter regions of the gastrointestinal tract.[12] i-scan images are as bright as conventional white-light images, therefore, i-scan is able to observe much larger areas from a distant view than NBI. Therefore, i-scan may be useful for evaluating not only oral cavity leukoplakia but also laryngo-hypopharyngeal lesion in head and neck area. Moreover, i-scan does not need magnifying endoscopy to observe the demarcation of the lesion. For evaluation of vascular characteristics on the lesion, i-scan tone enhancement (TE) dissects and analyses the individual red-green-blue (RGB) components of a normal endoscopic image in real-time, alters the color frequencies of each component, and recombines the components to a single, new color image without visible delay for the examiner. Thereby, TE enhances mucosal structures, vascular patterns and subtle changes in color. i-scan combines a variety of parameters to produce the effect of each i-scan mode. Among these are the following: brightness of light (off, -5 to +5), red (off, -5 to +5), blue (off, -5 to +5), light measuring mode (ave, peak) enhancement (off, low, med, high), surface enhancement (off, +1 to +6), contrast enhancement (off, +1 to +6) and tone enhancement settings (off, c, g, r, e, b, d).

To our knowledge this is the first study to investigate the diagnostic value of visual examination combined with i-scan for the diagnosis of oral cavity leukoplakia. This study shows that the use of i-scan image enhancement technology improves the detection of vascular changes, offering the combination of surface enhancement and tone enhancement. Huang et al. showed that microvessel characteristics in the mucosa around the plaque identified using NBI were closely associated with the pathological diagnosis.[13] Also, Yang et al demonstrated that the NBI images of twisted elongation of IPCL and IPCL pattern destruction are indicators of high-grade dysplasia or carcinomatous lesions in oral leukoplakia.[14] i-scan consists of three types of algorithms: SE, CE, and TE. SE and CE are expected to provide a useful means of screening because they can improve detection of lesions without altering the color tone markedly or reducing the brightness of images. After a lesion is found, TE is applied as a simple means of making changes in the color tone and structure more evident.[4] Hoffman et al. demonstrated that HD+ colonoscopy with i -scan functionality detected significantly more patients with colorectal neoplasia compared with standard resolution endoscopy.[15] In their study, significantly more neoplastic (adenomatous and cancerous) lesions and more flat adenomas could be detected using high definition endoscopy with surface enhancement. i-scan has proved useful not only in the intestinal mucosa but also in the airway mucosa. In an analysis of 29 patients, vascular abnormalities were scored most frequently in HD + i-scan 2 bronchoscopy than in autofluorescence videobronchoscopy. This study also showed that high definition bronchoscopy with image enhancement techniques may result in better detection of subtle vascular abnormalities in the airways.[16]

In our study, atypical blood vessels such as type IV abnormal worm-like vessels with spiral morphology and bizarre course were detected in leukoplakia lesions revealed as invasive carcinoma (Fig. 1). Perpendicular vascular networks are characterized by the development of IPCLs. The main target of analysis in i-scan techniques is neoangiogenesis, and observation of thick dark spots within a well-demarcated brownish area with proliferation of dilated and abnormal IPCLs is generally considered a hallmark of epithelial precancerous or neoplastic evolution. In most leukoplakic lesions proven to be malignant, abnormal IPCLs were detected on i-scan images. The growth of epithelial tumors leads to escalated disorderliness of the vascular microarchitecture, which is observed in practice as changes in the IPCL arrangement, diameter, and shape, and as a loss

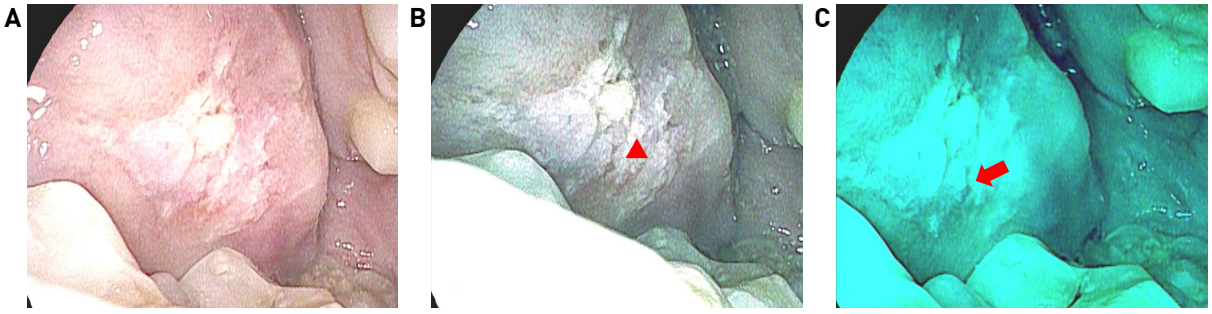

Fig. 1. Images using i-scan-enhanced endoscopy. A: i-scan 1 (surface and contrast enhancement, SE and CE). A whitish irregular lesion is seen on the left lateral border of tongue. B: i-scan 2 (SE, CE and tone enhancement (TE) c). i-scan 2 better demarcates the vascular components (arrow head) of a hypervascular lesion in oral cavity leukoplakia. C: i-scan 3 (SE, CE and TE v). i-scan 3 characterizes the abnormal vascular change with worm-like features (arrow).

of regularity.[7] Stanikova et al. demonstrated that 22/26 cases that had malignant IPCLs on NBI were confirmed to be carcinoma in situ or invasive squamous cell carcinoma.

i-scan SE highlights oral cavity mucosal surface structures that can be used for the detection of epithelial changes. Abnormalities are easier to detect. i-scan TE accentuates mucosal structures and vascular patterns, improving the determination of lesion margins. These details are helpful in demarcating and characterizing oral mucosa leukoplakia and degree of dysplasia. Neoplastic and inflammatory vessel and tissue patterns may be differentiated from non-neoplastic patterns. i-scan 3 (SE, CE and TEv) further enhances the visibility of the vessel patterns and helps in the localization of adequate biopsy sites.

This study has some limitations. First, we performed a retrospective image review, not prospective studies. There is a possibility that the description of the vascular pattern may be different depending on the part of the image taken. Second, in the present study we did not analyze surface mucosal change or epithelial abnormalities, which are important variables in endoscopic diagnosis. In future, prospective studies should be conducted to address these limitations and to validate the value of i-scan by comparing its efficacy with that of NBI.

Conclusion

Endoscopic image examination with an i-scan-enhanced technique is useful in detecting subtle vascular patterns in oral cavity leukoplakia. These vascular abnormalities could be significantly related to degree of dysplasia. Further studies for validating this technique for the diagnosis of oral cavity cancer are warranted.

References

1) van der Waal I. *Potentially malignant disorders of the oral and oropharyngeal mucosa; present concepts of management. Oral oncology. 2010;46:423-425.*
2) Isenberg JS, Crozier DL, Dailey SH. *Institutional and comprehensive review of laryngeal leukoplakia. Annals of Otology, Rhinology & Laryngology. 2008;117:74-79.*
3) Ni X, He S, Xu Z, Gao L, Lu N, Yuan Z, et al. *Endoscopic diagnosis of laryngeal cancer and precancerous lesions by narrow band imaging. The Journal of Laryngology & Otology. 2011; 125:288-296.*
4) Kodashima S, Fujishiro M. *Novel image-enhanced endoscopy with i-scan technology. World journal of gastroenterology: WJG. 2010;16:1043.*
5) Iacucci M, Poon T, Gui XS, Ghosh S. *High definition i-SCAN endoscopy with water immersion technique accurately reflects histological severity of celiac disease. Endoscopy international open. 2016;4:E540.*
6) Graham DG, Banks MR. *Advances in upper gastrointestinal endoscopy. F1000Research. 2015;4.*
7) Arens C, Piazza C, Andrea M, Dikkers FG, Gi RETP, Voigt-Zimmermann S, et al. *Proposal for a descriptive guideline of vascular changes in lesions of the vocal folds by the committee on endoscopic laryngeal imaging of the European Laryngological Society. European Archives of Oto-Rhino-Laryngology. 2016; 273:1207-1214.*
8) Barnes L, Eveson JW, Reichart P, Sidransky D. *Pathology and genetics of head and neck tumours: IARC; 2005.*
9) Ishii J, Fujita K, Komori T. *Laser surgery as a treatment for oral leukoplakia. Oral Oncology. 2003;39:759-769.*
10) Stevens SM, Johnson EA, Pfau PR, Dailey SH. *Visual evaluation of the larynx and hypopharynx during esophagogastroduodenoscopy: a safety and feasibility study. Surgical endoscopy. 2015; 29:1209-1215.*
11) Kuznetsov K, Lambert R, Rey J-F. *Narrow-band imaging: potential and limitations. Endoscopy. 2006;38:76-81.*
12) Yao K, Anagnostopoulos G, Ragunath K. *Magnifying endoscopy for diagnosing and delineating early gastric cancer. Endoscopy. 2009;41:462-467.*

13) Huang F, Yu J, Zhang F, He C, Li S, Shao J. *The usefulness of narrow-band imaging for the diagnosis and treatment of vocal fold leukoplakia. Acta oto-laryngologica. 2017;137:1002-1006.*
14) Yang SW, Lee YS, Chang LC, Hwang CC, Chen TA. *Diagnostic significance of narrow-band imaging for detecting high-grade dysplasia, carcinoma in situ, and carcinoma in oral leukoplakia. The Laryngoscope. 2012;122:2754-2761.*
15) Hoffman A, Sar F, Goetz M, Tresch A, Mudter J, Biesterfeld S, et al. *High definition colonoscopy combined with i-Scan is superior in the detection of colorectal neoplasias compared with standard video colonoscopy: a prospective randomized controlled trial. Endoscopy. 2010;42:827-833.*
16) van der Heijden EH, Hoefsloot W, van Hees HW, Schuurbiers OC. *High definition bronchoscopy: a randomized exploratory study of diagnostic value compared to standard white light bronchoscopy and autofluorescence bronchoscopy. Respiratory research. 2015;16:33.*