CASE REPORT

Reversal of pale-to-dark nasopharyngeal follicle ratio on narrow-band imaging

Alexander C Vlantis 屈力行
Amy BW Chan 陳碧雲
HS Chan 陳慶生
John KS Woo 吳港生
Michael CF Tong 唐志輝
C Andrew van Hasselt 尹懷信

Normal nasopharyngeal mucosa contains varying amounts of lymphoid tissue, which in adults may be minimal or absent. Nasopharyngeal mucosa with minimal lymphoid tissue has a regular follicular pattern on narrow-band imaging; pale follicles have thin, dark borders and the ratio of the pale follicle to the dark border (pale-to-dark ratio) is roughly 90%. In some patients undergoing routine nasopharyngeal endoscopy, the pale-to-dark ratio is reversed on narrow-band imaging, with dark centres surrounded by pale borders and a pale-to-dark ratio of roughly 50%. These dark follicles may represent abnormal capillary loops, as they have the same appearance as microvascular changes seen on narrow-band imaging of the oesophageal mucosa which indicate dysplasia or malignancy. While this observed change in the follicular pattern may be an early event in the evolution of nasopharyngeal carcinoma, the significance of this finding remains to be confirmed by a larger-scale study.

Introduction

The commonest presenting symptoms of nasopharyngeal carcinoma are an enlarged neck node or mass; nasal symptoms, such as unilateral nasal obstruction, blood-stained nasal secretions, or epistaxis; ear symptoms, such as unilateral hearing loss, tinnitus, and ear fullness; and blood-stained saliva.[1] Signs of nasopharyngeal carcinoma on endoscopy of the nasopharynx include an asymmetrical or eccentric mucosal covered fullness, ulceration, slough, blood and an obvious mass or tumour, which is usually exophytic, ulcerating or asymmetrical (Fig 1a and b).

The diagnosis of nasopharyngeal carcinoma is made histopathologically on biopsy of nasopharyngeal tissue. The endoscopist samples nasopharyngeal tissue, usually with biopsy forceps, to determine the pathology of any lesion seen. Assessing the nasopharynx for abnormal lesions is subjective and requires experience. Changes may be subtle, and lesions may be in the submucosa of an otherwise normally appearing nasopharynx.

Narrow-band imaging uses light in which the bandwidth has been narrowed, to illuminate the mucosa. The wavelength is shorter than standard white light. This shorter wavelength light is strongly absorbed by haemoglobin, which has an absorption peak of 415 nm, leading to a high contrast of blood vessels to surrounding non-vascular mucosal tissue.[2] Narrow-band imaging thus allows the endoscopist to assess the architecture of epithelial capillaries. This has proved useful in the detection of early oesophageal cancer, in which mucosal dysplasia is associated with changes in epithelial vessels.[3] Angiogenesis is essential for the transition of a premalignant to a malignant lesion, and so this ability to detect morphological changes in the microvessels of the mucosa has great potential benefit.[4]

Normal nasopharyngeal mucosa contains various amounts of lymphoid tissue (Fig 1c). Large amounts of lymphoid tissue in children and adolescents are known as adenoids, while nasopharyngeal lymphoid tissue may be minimal or absent in adults. Mucosal lymphoid tissue in adults has a regular follicular pattern on narrow-band imaging, in which pale follicles have a thin, dark border (Figs 1d and 2a). The ratio of the pale follicle to the dark border (pale-to-dark ratio) is roughly 90%.

The authors have noticed that this ratio is reversed in some patients undergoing routine nasopharyngeal endoscopy, with each 'follicle' consisting of a dark centre, surrounded by a pale border. The pale-to-dark ratio is in the order of 50%. This apparent reversal of the narrow-band imaging characteristics of nasopharyngeal mucosa appears similar to the abnormal capillary loop pattern seen on narrow-band imaging of early oesophageal cancer.[5] In the oesophagus, the increased microvascular density in the mucosa indicates dysplasia or malignancy, and is therefore an indication for biopsy.

An illustrative case is presented of a patient who had features of an abnormal capillary pattern on endoscopic narrow-band imaging of the nasopharynx, adjacent to a biopsy-proven carcinoma.

Key words
Biopsy; Carcinoma; Diagnostic imaging; Endoscopy; Nasopharynx

Hong Kong Med J 2010;16:307-9

The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong:
Department of Otorhinolaryngology, Head and Neck Surgery
AC Vlantis, FCS(SA)ORL
HS Chan, FRCSEd
JKS Woo, FRCSEd
MCF Tong, FRCSEd(ORL)
CA van Hasselt, MMed(Otol)
Department of Anatomical and Cellular Pathology
ABW Chan, FHKCPath

Correspondence to: Dr AC Vlantis
Email: lexvlantis@cuhk.edu.hk

窄頻影像系統顯示的鼻咽濾泡白色與深色部分的比例轉向

正常的鼻咽黏膜包含不同程度的淋巴組織，成人可能只有很少甚至無。鼻咽黏膜如果只有少量淋巴組織，在窄頻影像系統上會出現一種典型的濾泡形態，即白色濾泡被薄而深色的邊包圍，而白色與深色的比例約為9比1（90%）。接受常規鼻內窺鏡檢查的病人，其濾泡白色與深色的比例在窄頻影像系統上呈相反狀態，即是中間深色部分被白邊包圍，而白色與深色的比例參半（約50%）。由於食道黏膜發育不良或腫瘤的微血管異常在窄頻影像系統上會出現類似現象，這些深色濾泡可能代表著異常的血管環。要確認此濾泡形態轉變可能是鼻咽癌一個早期徵兆的觀察結果是需要的。

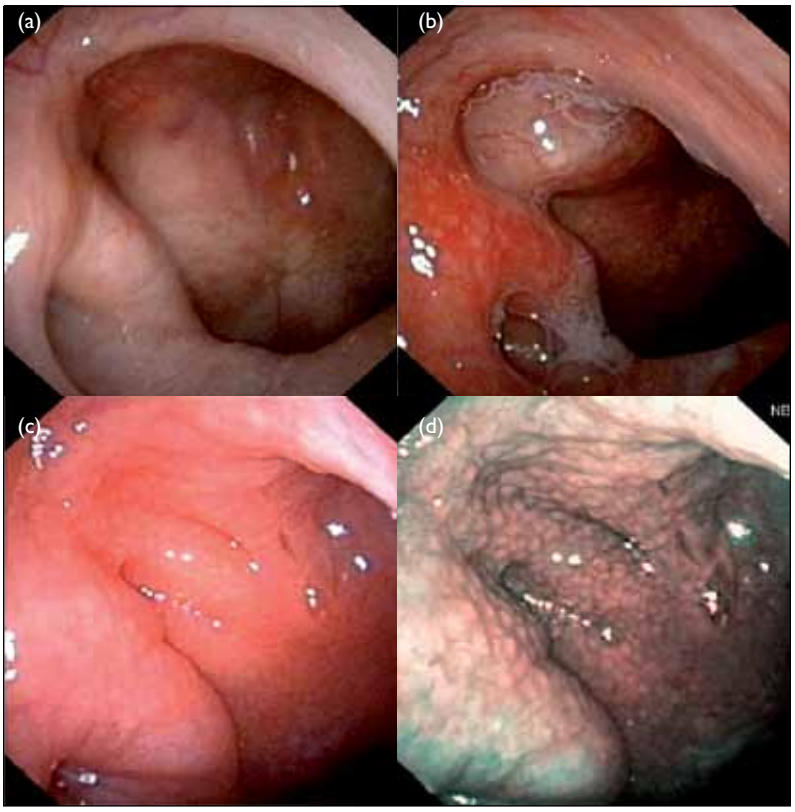

FIG 1. Endoscopic images of the right nasopharynx
(a) A normal nasopharynx; (b) an abnormal nasopharyngeal mass; (c) nasopharyngeal lymphoid tissue under white light; and (d) normal nasopharyngeal lymphoid tissue on narrow-band imaging showing a follicular pattern of pale follicles with thin, dark borders

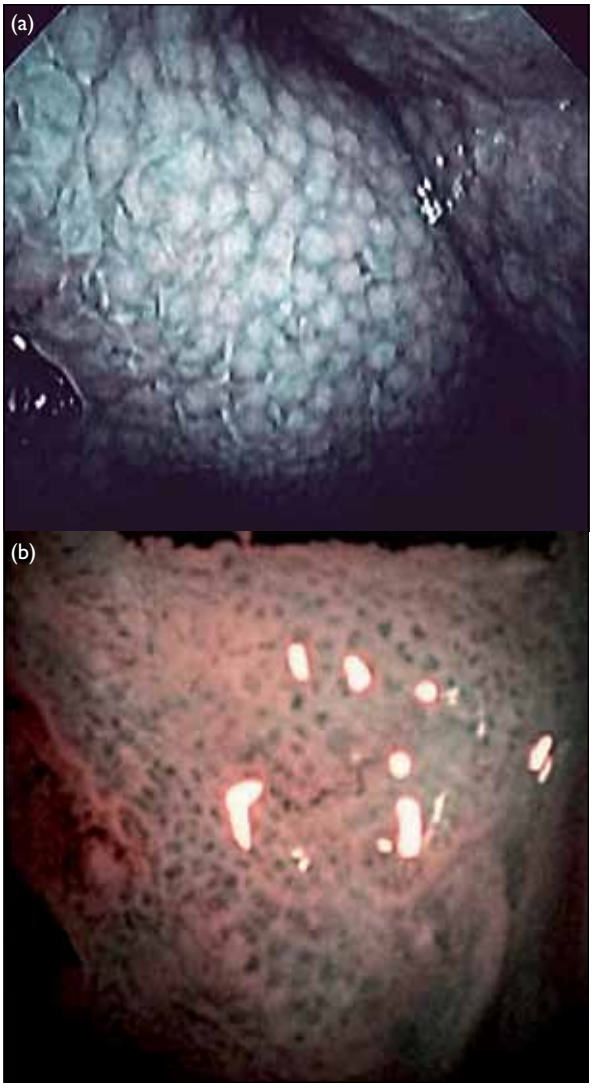

FIG 2. A magnified view of the nasopharyngeal mucosa on narrow-band imaging (x 10)
(a) Normal nasopharyngeal lymphoid tissue showing pale follicles with thin, dark borders; and (b) abnormal nasopharyngeal mucosa showing dark-centred follicles with pale surrounds

Case report

Nasopharyngeal endoscopy was performed on a 50-year-old man, who presented with vague nasal symptoms in February 2009. In Hong Kong, nasopharyngeal endoscopy is routine, due to the relatively high incidence of nasopharyngeal carcinoma. Narrow-band imaging identified an abnormal follicular pattern in the nasopharyngeal mucosa (Fig 2b). Each 'follicle' consisted of a dark central 'nucleus', surrounded by a pale 'cytoplasmic' halo. The ratio of the dark centre to the pale surround was about 50%. This abnormality is in contrast to the normal follicular pattern of nasopharyngeal mucosa, in which pale lymphoid follicles have a thin, dark reticular border. This area and adjacent mucosal abnormality was biopsied. Immunohistochemical antibody staining for the CD31 endothelial cell marker was done to highlight the endothelial components in the nasopharyngeal tissue. The adjacent mucosal abnormality was diagnosed as an undifferentiated carcinoma on histology.

Discussion

Inoue et al[6] reported that scattered red dots on a pinkish homogeneous background seen on ultra-

high magnification endoscopy are a common feature of carcinoma-in-situ of the oesophageal mucosa. They demonstrated that the red dots were abnormal, intra-epithelial papillary capillary loops, capillaries that were dilated, tortuous, had calibre irregularities or changes, and were of different shapes.[7] In oesophageal cancer, pre-existing epithelial capillaries elongate and dilate prior to new, immature vessels developing and proliferating.[8] Inoue[9] has shown that narrow-band imaging can recognise these abnormal intra-epithelial papillary capillary loops in oesophageal mucosa, and that a type IV pattern strongly suggests carcinoma-in-situ of the overlying epithelium. Narrow-band imaging specifically enhances the ability to assess the architecture of epithelial capillaries and so has proven useful in detecting early oesophageal cancers, which are associated with changes in epithelial vessels.[3] It is not yet known if the same is true for nasopharyngeal carcinoma. While the role of narrow-band imaging in the detection of early mucosal lesions of the hypopharynx is becoming established, its role in the detection of early lesions of the nasopharynx has not yet been defined.[3]

This report illustrates a case in which the usual pale-to-dark ratio of normal nasopharyngeal lymphoid mucosa is reversed. The abnormal vascular pattern is very similar to that associated with dysplasia or carcinoma-in-situ of the oesophageal mucosa on narrow-band imaging. Histology of the mucosa with abnormal vessels and reversed pale-to-dark ratio showed increased vascularity on CD31 immunohistochemical staining and the adjacent mucosal lesion showed undifferentiated carcinoma.

Further insights into tumour vasculature will hopefully lead to the future development of novel therapeutic approaches, not only for oesophageal carcinoma but for many other types of tumours, including nasopharyngeal carcinoma.[8]

Endoscopic detection of gastro-intestinal lesions depends on the recognition of visible mucosal changes. Similarly, the endoscopic detection of early nasopharyngeal carcinoma depends on the recognition of visible mucosal changes or asymmetry of the underlying submucosa, and hence has limitations. The use of narrow-band imaging to detect a reversal of the pale-to-dark ratio of nasopharyngeal follicles in otherwise normal nasopharyngeal mucosa may serve to signal an early event in the evolution of nasopharyngeal carcinoma. The significance of these imaging findings remains to be confirmed by a larger-scale study.

References

1. van Hasselt CA, Leung SF. Clinical picture. In: van Hasselt CA, Gibb A, editors. Nasopharyngeal carcinoma. 2nd ed. Hong Kong: The Chinese University Press; 1999: 105-10.
2. East JE, Guenther T, Saunders BP. Novel approaches in colorectal endoscopy: what do we need biopsies for? Pathol Res Pract 2008;204:459-67.
3. Kozu T, Saito Y, Nonaka S, Saito D, Shimoda T. Early detection of hypopharyngeal cancer by narrow-band imaging. Dig Endosc 2006;18(Suppl):6S-8S.
4. Muto M, Horimatsu T, Ezoe Y, et al. Narrow-band imaging of the gastrointestinal tract. J Gastroenterol 2009;44:13-25.
5. Kumagai Y, Inoue H, Nagai K, Kawano T, Iwai T. Magnifying endoscopy, stereoscopic microscopy, and the microvascular architecture of superficial esophageal carcinoma. Endoscopy 2002;34:369-75.
6. Inoue H, Honda T, Nagai K, et al. Ultra-high magnification endoscopic observation of carcinoma in situ of the esophagus. Dig Endosc 1997;9:16-8.
7. Inoue H, Kumagai Y, Yoshida T, Kawano T, Endo M, Iwai T. High-magnification endoscopic diagnosis of the superficial esophageal cancer. Dig Endosc 2000;12:32S-35S.
8. Kumagai Y, Toi M, Inoue H. Dynamism of tumour vasculature in the early phase of cancer progression: outcomes from oesophageal cancer research. Lancet Oncol 2002;3:604-10.
9. Inoue H. Endoscopic diagnosis of tissue atypism (EA) in the pharyngeal and esophageal squamous epithelium; IPCL pattern classification and ECA classification [in Japanese]. Kyobu Geka 2007;60:768-75.