Case Series

Application of high-resolution narrow band imaging and endocytoscopy for early diagnosis of esophageal neoplasia

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The worldwide incidence of esophageal carcinoma has been rising rapidly over the past few decades. However, in only 31% of patients the carcinoma is detected early in situ. It is essential to detect the malignancy early and to determine the extent of the disease to ensure the best option for a cure. Recent advances in endoscopic technology, including high-resolution magnification endoscopy, narrow-band imaging and endocytoscopy, have increased detection rates of oesophageal microcarcinomas. We report three cases of esophageal malignancy where the use of newer diagnostic techniques ensured an early diagnosis which led to a modified course of management.


We describe three cases of early esophageal malignancy in which these newer diagnostic techniques helped make an early diagnosis, thereby making it possible to revise the management of the disease.

Case Reports

Case 1
A 65-year-old man presented with mid chest discomfort and uneasiness. Cardiac evaluation was normal. Endoscopy revealed a small 1 cm x 1 cm lesion with nodularity and superficial erosions (Figure 1A). A biopsy was taken which was positive for superficial squamous cell carcinoma. An endoscopic ultrasound (EUS) confirmed the superficial nature of the disease, with no involvement of the underlying layers. EMR was planned.

NBI with magnification of the same lesion identified an extended area of desquamation, with few dilated intrapapillary capillary loops (IPCLs) (Type IV; Figure 1B). Endocytoscopy was done before EMR, after staining the area with methylene blue. A focus of atypical cells was detected 5 cm beyond the macroscopic involved area. The margins of the involved area were marked and a biopsy was taken. Histology confirmed malignant cells in the specimen. An endoscopic mucosal resection was performed for both the areas and free margins were confirmed by histopathology.

Case 2
A 56-year-old man presented with severe reflux symptoms for over a month; he had had mild symptoms for over a year and was on intermittent proton pump inhibitor (PPI) therapy. An upper GI endoscopy performed earlier had revealed superficial ulcerations at the lower end of the esophagus (at 35 cm). A biopsy of this area revealed chronic inflammation.

NBI of the same area revealed a central avascular area of
necrosis (approximately 1 cm) with destroyed capillary network and peripheral abnormal vessels with dilated IPCLs (Types IV and V; Figure 2) at 6 o’clock position. The remaining circumference appeared normal. Targeted biopsy from the same area revealed atypical cells suggestive of squamous cell carcinoma. Endosonography revealed a peri-esophageal node in the same area. The patient was referred for chemoradiation followed by surgery.

**Case 3**
A 46-year-old woman with dysphagia for 6 months was noted to have a mild hyperemic patch (2 cm) with prominent margins in the distal esophagus on standard white light endoscopy. The rest of the examination was normal. Magnification endoscopy with NBI revealed a mild nodularity in the hyperemic patch and multiple dilated IPCLs (Types IV and V) extending approximately 1 cm beyond the margin. Neoplasia was suspected.

An endocytoscopic examination was performed to assess the type and extent of the lesion. The mid esophagus, including the suspicious area, was sprayed with 1% methylene blue. The prototype 1 Endocytoscope (Olympus Corporation, Tokyo, Japan), was then inserted through the working channel of the endoscope (Olympus GIF-160) to examine this area. A large number of atypical cells, which were clustered together with hyperchromatic nuclei and a high nuclear: cytoplasmic ratio, suggestive of neoplasia (Figure 3A), were seen. The normal area showed a regular arrangement of cells with a normal nuclear: cytoplasmic ratio (Figure 3B). An EUS and CT of the chest did not reveal any metastasis or submucosal infiltration. The margins of the lesion were then marked with an APC probe and an endoscopic mucosal resection performed. A biopsy of the resected specimen confirmed the diagnosis and showed clear margins. The patient is asymptomatic 10 months post-procedure with complete healing on surveillance endoscopy, including NBI.

**Discussion**
Recent advances in endoscopic imaging modalities include magnification endoscopy, NBI, autofluorescence, optical CT, confocal endoscopy and endocytoscopy.\(^3\)

The NBI system is a sequential electronic system, which uses optical filters to examine the mucosal morphology. RGB filters with narrow-band pass ranges, and a higher relative intensity of blue light are used. They enhance the contrast and enable better visualization of mucosal patterns and superficial vasculature.\(^6\)

The squamous epithelium of the esophagus appears featureless on NBI. NBI defines a fine vascular network pattern with regularly arranged IPCLs. These IPCLs show characteristic changes, including dilatation, weaving, irregular caliber and an alteration in shape in dysplasia and carcinoma \textit{in situ}, and have accordingly been graded from Type I (normal) to Type V (carcinoma).\(^5\) On conventional endoscopy most of these small cancers and microcarcinomas appear faint red in color, which is similar to the color of many innocuous and benign lesions. Hence a targeted biopsy of lesions based on this finding alone can be futile. NBI can now clearly demarcate and identify the involved area.\(^7\) Recent studies have shown excellent coordination of NBI with histopathology.\(^8\)
Endoscopy techniques for early diagnosis of esophageal cancer

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For endoscopy, we used the prototype Endocytoscopy system consisting of a soft flexible catheter type endoscope, which can be passed through the working channel of a conventional endoscope. On contact with tissues stained with vital dyes, like methylene blue, it provides a real-time 450x magnification allowing cellular level observation in vivo. The normal cells are arranged homogeneously with a normal nuclear:cytoplasmic ratio. Mitotic cells, on the other hand, appear heterogeneous in shape with altered nuclear:cytoplasmic ratio, and are arranged in irregular clusters (Figures 3A, 3B).

Early detection is the key to successful management of esophageal malignancy.10 The three cases we have presented reflect the advantages of high-resolution magnification endoscopy with NBI, and endocytoscopy in the early detection of esophageal carcinoma. However, results in an individual patient cannot always be generalized. There are challenges before these novel technologies can be accepted into clinical practice.10 Personal skills and experience affect detection and diagnostic ability. A major disadvantage of NBI and the endocytoscopy is the presence of mucus or blood in the tissue being scrutinized. This can obscure the view. Respiratory and cardiac movements also hamper visualization.

It is difficult to map the precise area of involvement with the endocytoscope as the entire malignant area cannot be observed at the same time. Moreover, it is not easy to interpret the histological nature of a lesion from pictures taken by the endocytoscopy system. Images were interpreted in real-time by an experienced cytopathologist and confirmed by conventional biopsy. Systematic additional training may be required before endoscopists can interpret pathology slides conclusively.

The above cases highlight the usefulness of the newer technologies in the management of esophageal malignancy. The NBI system is easy to use and interpret and could be a useful adjunct to regular white-light endoscopy. The endocytoscopy system makes microscopic observation possible at the cellular level and may assist tissue characterization in a variety of esophageal lesions.

References

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