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Contact endoscopy of the larynx: a quantitative study

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Abstract

Contact endoscopy is a technique of obtaining detailed magnified images of living epithelium, using a modified glass rod lens endoscope placed on the surface of the tissue. The technique has been extensively described in gynaecological, and more recently, laryngeal and nasal tissues. However, no quantitative studies of its diagnostic accuracy yet exist. A prospective partially blinded controlled study of eight cases with a variety of laryngeal pathologies is described. A single pathologist with no knowledge of the ultimate histological diagnoses successfully identified six of eight laryngeal pathologies on contact endoscopic findings, while the other two cases were identified to a degree of accuracy that was sufficient to positively identify the need for standard tissue biopsy. The advantages and disadvantages of the technique are described, along with suggestions for its role in clinical practice.

Key words: Larynx; Endoscopy; Histology, comparative

Introduction

Any technique which gives histological information without damaging tissues has obvious advantages over biopsy. Indeed, less invasive methods of sampling tissues, such as fine needle aspiration cytology (FNAC), sputum and cervical cytology have gained widespread popularity in the latter half of this century, and have found a place alongside biopsy in clinical and screening practice. The main problem with these less invasive methods of histology is their reliability and difficulties in their interpretation, that is more demanding for the histologist. Biopsy remains the 'gold standard' to which they are compared.

The vocal folds have a very specialized and delicate microstructure[1] that is intolerant of even slight trauma, yet histology is often crucial in the management of mucosal disorders of the larynx, particularly in the management of carcinoma and dysplasia. Indeed the only reliable way to monitor the progress of the latter has been by repeated biopsies over many years, since progression is often asymptomatic for the patient and invisible to the endoscopist. A technique which allows monitoring of dysplasia without recourse to repeated biopsy of the vocal fold would clearly be advantageous.

The contact endoscope was developed of Hamou in the early 1980s for gynaecological use[2] and 10 years later was adapted by Andrea and Dias for use on vocal fold epithelium.[3] These authors have since documented its use for a wide range of laryngeal[3–5] and, more recently, nasal disorders.[6]

The laryngeal version of the device is 23 cm long and will fit comfortably through a Kleinsasser laryngoscope. It resembles, and works like, a Hopkins Rod rigid endoscope, but has an additional focusing and magnification selection dial.

In order to investigate the accuracy of this technique in laryngeal mucosal pathology, we carried out a prospective, partially blinded controlled study where contact endoscopic findings in a variety of pathologies were determined and then compared to standard histological sections of the same sites.

Patients

Eight consecutive adult patients due to undergo microlaryngoscopy and biopsy in a teaching hospital otolaryngology unit were asked to participate in this study. A variety of laryngeal mucosal disorders were included. Informed consent was obtained and ethical approval sought from the regional ethics committee. Children under 16 and those unwilling or unable to give informed consent were excluded.

Methods

A standard Kleinsasser microlaryngoscopy setup and general anaesthesia were used in all cases. The larynx was examined under the microscope and the area of interest painted with 0.5 ml of one per cent methylene blue using a syringe and spinal needle. (No adverse effects of the methylene blue were observed during the procedure or the recovery,

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TABLE I
COMPARISON OF CONTACT ENDOSCOPIC AND HISTOLOGICAL FINDINGS AND DIAGNOSES IN EIGHT CASES OF LARYNGEAL PATHOLOGY

Patient	Contact endoscopy	Histology	Clinical appearance (unknown to pathologist)
(a)	Crowded cells, nuclei with a twisted contour in empty cytoplasm (koilocytes), vasculature viewed *en face* in a papilliferous architecture *Squamous papilloma*	Papilliferous architecture no keratin, koilocytes present *Viral squamous papilloma*	Discreet papilliferous lesions
(b)	Crowded, irregular cells enlarged nuclei, keratin sheets, no koilocytes *Dysplastic keratosis*	Variation in cell layer thickness loss of basal alignment nuclear variation dyskeratosis, mitoses *Moderate/severe dysplasia*	Leukoplakia on true vocal fold
(c)	Uniform cells slight nuclear size variation no neoplastic vasculature regular architecture no keratin or koilocytes *Normal epithelium*	Cells in basal layer showed slight variation in nuclear size secondary blood vessel dilatation keratin formation *Haemangioma*	2 mm cherry-red nodule
(d)	Tortuous vasculature keratin formation no koilocytes *Carcinoma*	Ulcerated squamous carcinoma Angioneogenesis Invasive carcinoma	Ulcerating tumour in pyriform fossa
(e)	Disordered, crowded cells enlarge nuclei parakeratosis, no koilocytes *High grade dysplasia*	Squamous carcinoma *Squamous carcinoma*	Ulcerating tumour on supraglottis
(f)	Crowded cells, nuclear enlargement variable morphology keratin formation no koilocytes *Squamous carcinoma*	Fragments of carcinoma parakeratosis full thickness dysplasia necrosis, ulcerated *Squamous carcinoma*	Ulcerating tumour on true vocal fold
(g)	Crowded cells, mild nuclear size variation, keratin production no koilocytes *Moderate dysplasia*	Keratosis, moderate dysplasia some inflammatory features fibrin in stroma *Moderate dysplasia*	Leukoplakia on true vocal fold
(h)	Cell relationship slightly abnormal minimal nuclear enlargement non-neoplastic vessels keratin production *Keratosis, mild dysplasia*	Increased cellularity disordered maturation Suprabasal mitoses *Mild to moderate dysplasia*	Reddened area on true vocal fold

although some of the patients noticed blue tingeing of their saliva for one to two hours after return to the ward.) The Storz 8715A contact endoscope was guided down the Kleinsasser laryngoscope towards the larynx until touching the exact area of interest. The surgeon has a typical endoscopic overview of the larynx through the contact endoscope on the low power setting. This allows exact placement upon the area of pathology. The contact endoscope was then refocussed under low (× 60) and high (× 150) power and still photographs taken using the Storz Endovision Telecam camera, a Storz Xenon 300 light source and a computerized photographic video capture system (Hauppage Win-TV). Six to eight stills were taken for each patient and recorded on floppy disc. Biopsies of the same sites were then performed using standard Kleinsasser microlaryngeal instruments. These biopsies were then sent for histological examination.

A single pathologist with no knowledge of the ultimate histological diagnoses was then asked to analyse the contact endoscopic photographs for each patient. Characteristics analysed included cell and nuclear regularity, cell to cytoplasm ratio, regularity of vasculature and the presence or absence of koilocytes and keratin. No clinical information was given to the pathologist. A diagnosis was offered in each case. The same pathologist then reviewed the histological slides in random order, and without reference to patient identity or clinical details. The diagnoses from histology and contact endoscopy were compared (Table I).

Results

The contact endoscopic and histological findings for each patient are summarized in Table I. The images from patient (c) were wrongly diagnosed as normal epithelium, probably because the epithelium itself *was* normal and the abnormality lay below the

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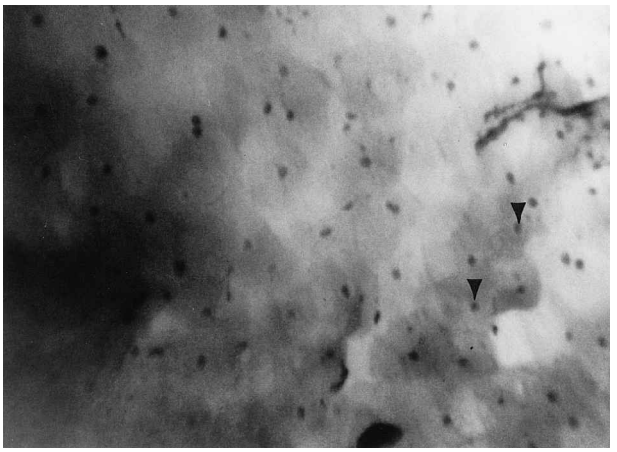


FIG. 1

Normal vocal fold epithelium on contact endoscopy (case c) Note regular cell and nuclear characteristics (nuclei arrowed) (Methylene blue; ×150).

surface. Patient (e) was assessed as having high grade dysplasia dictating the necessity for biopsy, which showed squamous carcinoma. This highlights the fact that contact endoscopy images tissues in a 'face-on' plane rather than a cross section, and thus relies on cell and nuclear morphology rather than assessing the depth of an abnormality.

Discussion

Due to the limited availability of the prototype instrument, the sample size of this study was limited to a two-month time frame. Despite this, the high diagnostic accuracy of the contact endoscopic pictures is substantiated by the blinding and controlled design of this study. Although the pathologist may have had *some* idea of the histology to follow after interpreting the contact endoscopic pictures, the slides were reviewed anonymously and in random order. Furthermore, ensuring that the same pathologist analyses all the specimens ensures consistency of interpretation.

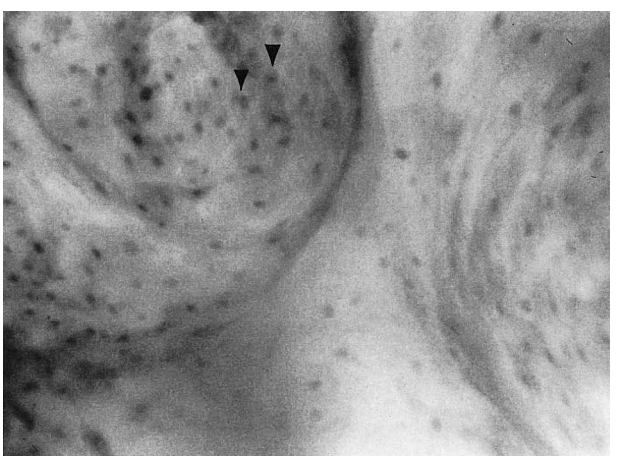


FIG. 2

Papilloma (case a) showing papilliferous architecture with cells arranged in whorls. Koilocytes (ballooned cells with nucleus pushed to periphery) arrowed (Methylene blue; ×150).

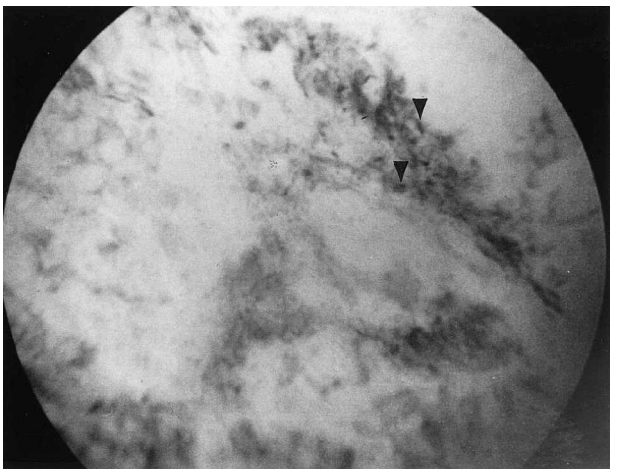


FIG. 3

Carcinoma (case f) showing cellular and nuclear pleomorphism (pleomorphic cells arrowed) (Methylene blue; ×60).

Some of the photographs were of poor quality and most cases required five or six to be taken in order to obtain a representative picture of each tissue. The pathologist was interpreting contact endoscopic pictures for the first time, with reference to an atlas of standard appearances.[5] Accuracy could be expected to improve with experience. Similarly, the endoscopist needed to familiarize himself with the technique of placing the endoscope, and deciding whether a representative image of sufficient diagnostic quality had been obtained. This 'learning curve' has been observed with other minimally invasive diagnostic techniques.

It is of interest that the pathologist correctly identified the degree of dysplasia in two out of three cases, both of which were of a degree one would not expect to be detectable on the surface. Assessing the degree of dysplasia represents a particular problem, since this is currently defined by the vertical height that the abnormal cells extend above the basal layer on cross section. Although epithelium is transparent and all its layers and indeed the submucosal vessels can potentially be visualized by contact endoscopy, methylene blue is only thought to penetrate the top layer of cells. Nonetheless the pathologist correctly identified the degree of dysplasia in cases (g) and (h) even though these are by definition not seen on the surface in standard histology. Given the complex three-dimensional undulation of epithelium, it may be that deep layer abnormalities are expressed on the surface by morphological features not seen on cross sectional histology. Patient (e), who was shown on biopsy to have invasive carcinoma, showed the expected surface high grade dysplasia from which tumour derives, but the diagnosis of invasion was not detected. Pleomorphism of this degree on contact endoscopy should in any case prompt the clinician to take a standard biopsy.

An added dimension to this technique is the analysis of submucosal vasculature. The irregular size, shape and pattern of the vessels in case (d) assisted in the diagnosis of frank malignancy.

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Papillomata too have a characteristic telangectatic vasculature. When viewed *en face* the vessels in the papillary core are evenly spaced.

The non-traumatic nature of this technique makes it ideal for delicate vocal fold mucosa, particularly in the case of voice professionals and those likely to require repeated regular biopsies, e.g. patients with laryngeal dysplasia. Mapping tissue abnormalities when deciding tumour resection represents another potential application. Its use in other tissues in the head and neck, such as the nasal and oral cavities, has been described;[6,7] indeed these more accessible sites would not require general anaesthesia and would be suitable for out-patient use. Because living epithelium is seen the clinician can get a truer view of the tissues, avoiding processing artefacts; indeed new diagnostically useful features not seen in processed samples may come to light.

The technique, of course, has disadvantages. Some submucosal pathologies, such as cysts, may not be seen. Vocal fold nodules have yet to be fully assessed by this technique. Since these are surface phenomena, the endoscope may aid in their differentiation from cysts, although these pathologies were not studied in our sample and a further series will be required to address this issue. The lack of depth perception with the two-dimensional image denies the clinician important information by which invasion and dysplasia are presently quantified. One would not, for example, rely solely upon a contact endoscopic diagnosis in cases of suspected carcinoma, however, the main advantage of the technique, i.e. atraumatic tissue analysis, is not a priority in such cases. As in other minimally invasive diagnostic techniques, its place would be as an adjunct to biopsy, replacing it only in specific instances, pending confirmation of reliability.

The technique currently relies upon rigid lens technology, so a clear view of the larynx is required and it would not be suitable for 'difficult' endoscopies unless a fibre-optic version were to become available.

Other disadvantages include the inability to study the nature of chromatin in individual cells, a significant criterion in the assessment of dysplasia. Moreover, ancillary techniques such as antibody labelling are precluded.

In the future some of the disadvantages of the contact endoscopy may be overcome by advances in other technologies. Improvements in computer graphics will allow higher quality imaging to complement the undoubted versatility afforded by the digital image capture system used in this study; unlike standard photography, images can be immediately reviewed for selection and storage, or live review by the pathologist if telemedicine facilities are available.

Conclusions

This small, partially blinded controlled study gives encouraging results as to the accuracy of this novel technique in laryngeal pathology. We suggest that this method of laryngeal assessment be pursued further. An increase in the number and range of cases should allow elucidation of those criteria most reliably detected by both contact endoscopic and histopathological techniques. Thereafter the place of this new technology in the investigation, diagnosis and follow-up of laryngeal abnormalities may be established with greater confidence. Contact endoscopy represents a novel and exciting advance in minimally invasive tissue analysis and documentation, but its place in clinical practice will only be assured if its reliability can be proven and its limitations fully understood.

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