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The Novel Use of the Micro-Endoscope to Diagnose Oral Lichen Planus: A Case Study

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Abstract: Lichen planus is a common dermatologic disease. In the oral cavity, lichen planus can appear on any mucosal surface, the most common areas are the posterior buccal mucosa and the tongue. Oral lichen planus (OLP) affects approximately 0.5-2% of the population. We present our experience using a specialized Hopkin's rod, the micro-endoscope, which provides magnified images of up to 150 times that allows a detailed examination of pre-stained mucosal surface. We also present a practical office methodology for the use of this scope in the clinical practice. The micro-endoscopic appearance of the lesion correlates very well with the typical histological appearance of lichen planus. The micro-endoscopic appearances were markedly different from those of squamous cell carcinoma.

Key words: Oral lichen planus, micro-endoscopy, diagonose, disease

INTRODUCTION

Oral Lichen Planus (OLP) is a chronic inflammatory oral mucosal disease that is related to a cell-mediated immune process (autoimmune disease). The prevalence of the oral lesions in the general population has been variously reported as being between 0.5 and 2% (Renata-Rodrigues *et al*., 2005; Scully and el-Kom, 1985).

The histopathologic features of OLP include several epithelial changes, the amount and extension of which vary. Epithelial hyperkeratosis, atrophy or hyperplasia, acantosis, saw-toothed rete ridges, liquefaction degeneration of basal cells and single-cell keratinization are all prominent characteristics. A homogeneous cell-free zone is frequently present in the basement membrane zone. The subepithelial connective tissue shows a band-like inflammatory infiltrate dominated by lymphocytes and macrophages (Andreasen, 1968).

Biopsy is obviously an important tool in the diagnostic process for OLP (Barnard *et al*., 1993), but a diagnosis of OLP based solely on histopathology in some cases leads to an erroneous result that emphasizes the well-known problem of subjectivity resulting in intra- and interexaminer variation among pathologists (Van der Meij *et al*., 1999).

The possible malignant transformation of Oral Lichen Planus (OLP) is the subject of an ongoing and controversial discussion in the literature. Hallopeau (1910) first described a case of carcinoma arising in lichen planus of the oral mucous membrane. Ever since, several mainly retrospective studies and case reports have been published on this subject (Erik *et al*., 2003).

The range of malignant transformation of OLP per year, as described in the literature, varies between 0.04 and 1.74%. Some authors have therefore accepted that OLP is of a premalignant nature. However, Krutchkoff and colleagues have criticized this opinion. Their criticism was largely that there were insufficient data to support the initial diagnosis of OLP. Krutchkoff and Eisenberg have stated that some of the reported OLP cases developing oral cancer were in fact not OLP, but rather dysplastic lesions with lichenoid features (Krutchkoff *et al*., 1978; Eisenberg and Krutchkoff, 1992).

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It is presently the goal of several developments in diagnostic instrumentation to enable real-time histology or virtual biopsy at the time of examination. For diminutive lesions or microscopic abnormalities amidst large fields of diffuse disease, biopsy targeting and adequate sampling can be difficult and time consuming. Various authors have tried to adapt gynecologic methods of examination to the oral cavity, but with limited success (L'Estrange *et al*., 1989; Kellokoski *et al*., 1990).

Contact endoscopy was first introduced by Hamou in 1979, as microhysteroscopy, to examine the surfaces of the genital tract at high magnification (Hamou, 1980, 1981, 1983).

The instrument is designed so that its tip can make direct contact with the tissue surface and visualize its superficial cells at high magnifications, thereby allowing *in-vivo* and *in-situ* examination of epithelial cellular morphology. Contact endoscopy has also been applied to visualize superficial cells of various pathologies in the larynx. The characteristics of chronic laryngitis, keratosis, dysplasia and invasive squamous cell carcinoma of the vocal cords obtained by contact laryngoscopes have been well described(Andrea *et al*., 1995).

The ability to obtain such images *in vivo* and at near real time suggests several potential clinical applications for microendoscopy such as non-invasive diagnosis of oral lesions and the ability to determine tumor margins *in vivo* in real time. Visual inspection and palpation remain the standard methods used to assess the extent of mucosal involvement by carcinomas and premalignant lesions. However, molecular and pathological assessments of "normal-appearing" mucosa have revealed molecular and cellular changes in these tissues, illustrating the fallibility of visual detection of dysplasia even by highly trained clinicians(Brennan and Sidransky, 1996).

To compensate for the limitation of surgeons to exactly determine the margins of carcinoma or dysplasia, it is accepted practice to resect a large cuff (approximately 1-2 cm) of normal-appearing mucosa around the visibly abnormal tissue. This produces better likelihood of complete excision but increased postoperative morbidity due to the greater amount of tissue removed.

In this study, our experience in the diagnosis of OLP lesion by contact endoscopy is reported. We believe it is the first report of contact endoscopic findings of OLP of the buccal mucosa in the literature.

CASE STUDY

A 42 years old white male was referred to The Royal National Throat, Nose and Ear Hospital for examination of a white lesion on the right buccal mucosa associated with an intermittent burning sensation and had been present for the last 3 months. The patient was otherwise well and he was taking no medication. He did not drink alcohol, smoke tobacco, or chew areca nut. No history of trauma or surgery in the area of the white lesion and no familial history of similar disease were reported. He denied a previous history of similar mucosal or skin lesions.

Clinical examination revealed a depigmented white lesion on the right buccal mucosa with evident whitish striae extending from the distal aspect of the mandibular right second molar to the labial aspect of the mandibular right canine (Fig. 1). The lesion was approximately 2×5 cm in size and on palpation it was firmer than the surrounding areas. The patient's oral hygiene was good.

The patient was examined with the micro-endoscope in the out-patients department; the area of interest was inspected and then cleaned of excess saliva.

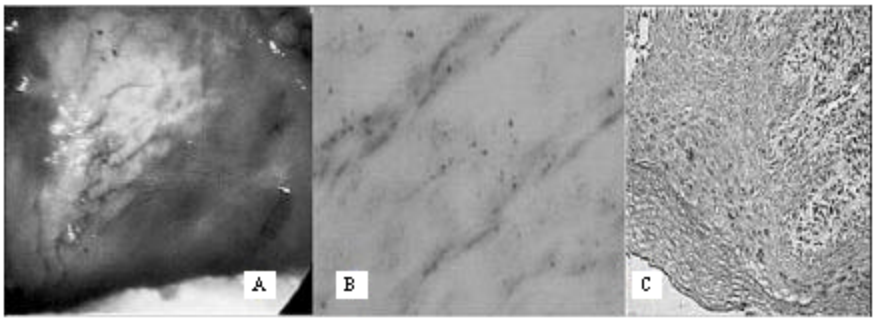

Fig. 1: A: Oral Lesion stained with diluted Methylene Blue (1%). B: Micro-image of the surface mucosa (150×magnification). C: Buccal mucsal specimen (200×magnification) showing intact stratified squamous epithelium demonstrates saw-tooth like rete ridges. This epithelium overlies a submucosal that contains a band like collection of chronic inflammatory cells composed of lymphocytes. Hydropic degeneration of the basal layer is also evident

An independent clinician who noted the representative site for biopsy according to clinical criteria also examined the whole of the mucosal surface of the lesion.

Diluted Methylene blue dye (1%) was applied to the area of the lesion with a cotton bud. Excess dye was suctioned away. The micro-endoscope used was a Storz Hopkins II; 30o Forward oblique endoscope (4 mm diameter and 18 cm long) attached via a Storz fibre optic cable to a Halogen light source. The eye piece was connected to a 3 chip Olympus camera and Video monitor. Photographs were taken using a Sony video photoprinter. After suction clearance, the tip of the micro-endoscope was firmly applied to the area of interest to obtain an occlusive contact and then moved for dynamic assessment of the mucosal lesion and its underlying vasculature and blood flow. The micro-endoscope tip was applied to the stained buccal mucosa and the image recorded after magnification and focusing.

Using a local anesthetic technique a biopsy was then taken from the most representative site of the lesion as shown by micro-endoscopy; further biopsy was taken from the edge of the lesion. The micro-endoscopic images were then examined by 2 independent head and neck pathologists and found to be highly suggestive of oral lichen planus; this was later confirmed by later histological analysis.

The characteristic microscopic features of the oral lichen planus were recognizable in both the images obtained with the micro-endoscope and those by traditional light microscopic examination of the biopsy specimen (Fig. 1).

RESULTS AND DISCUSSION

In the past, scientists have investigated several histochemical markers to determine their relevance as prognostic tools in the evaluation of OLP, epithelial dysplasia and oral cancer. These include altered expression of alpha9 integrin and laminin-5 staining (Hakkinen *et al*., 1999; Kainulainen *et al*., 1997). Involucrin immunoreactivity has also been proposed as a method to distinguish between lichen planus and lichenoid dysplasia (Eisenberg *et al*., 1987).

Using microsatellite analysis to elucidate the pre-malignant potential, Zhang *et al*. (1997, 2000) reported that lichenoid lesions with mild dysplasia showed a higher loss of heterozygosity (54%) as compared with OLP (6%).

A recent study showed that the DNA content was a powerful predictor of the risk of malignant transformation of the lesion (Sudbo *et al*., 2001). Surprisingly, the degree of dysplasia did not correlate with DNA content or the risk of cancer. Studies are warranted to evaluate this method as a predictor for malignant transformation of OLP lesions. The use of test methods such as vital staining with toluidine blue and brush biopsy (cytology) may enhance the possibility for the identification of signs of dysplasia or carcinoma in existing lesions (Epstein and Scully, 1997; Handlers, 2001). Therefore, in certain situations, they may serve as alternatives to biopsy in recall systems, although the value of toluidine blue staining was questioned in a recent study (Mignogna *et al*., 2001).

For the minimization of morbidity and mortality as a consequence of malignant transformation of OLP, an early identification of oral cancer and its precursors has been considered as important (Scully and Ward-Booth, 1995; Scala *et al*., 1997). In that regard, recall systems for OLP have been proposed to include professional examination 2-4 times annually or once a year (Duffey *et al*., 1996; Scully *et al*., 1998).

This study demonstrated that it is feasible to acquire instant *in vivo* histologic imaging by using micro-endoscopy. The images have sufficient resolution and contrast to distinguish cellular and some subcellular structures of interest at the time of examination.

The rapid, noninvasive nature of this technique also allows examination of a greater number of sites than can feasibly be excised. The length of time to obtain a single-site sample of microscopic information is significantly less than for conventional biopsy. Furthermore, many site samples can be collected in a unit of time comparable with that taken for biopsy and the clinician has the flexibility to cluster or to scatter the targeting of multiple samples. Micro-endoscopy thus offers appealing sampling statistics to increase the probability of clinical diagnosis. Moreover, this procedure is free of biopsy-associated bleeding or tissue damage. Another advantage of micro-endoscopy is the elimination of the delays associated with conventional biopsy-tissue preparation and processing, enabling *in vivo* microscopic assessment at the time of patient examination.

Recently, contact endoscopy proved to be an accurate technique in differentiating normal cells of the nasopharynx from malignant cells and allows an *in vivo* diagnosis of primary NPC in a clinical setting (Martin-Wai *et al*., 2001). Moreover, contact endoscopy may play 2 important roles in the routine surveillance of patients who have received radiotherapy. First, it directly identifies persistent and recurrent disease even in the presence of a normal-appearing nasopharynx. Second, it helps to direct the site of biopsy at the suspicious areas with cellular atypia. It not only helps to improve the

diagnostic yield of the biopsy but also potentially avoids the need for multiple-punch biopsies (Martin-Wai *et al*., 2001). They concluded that contact endoscopy can be used as an office-based procedure to confirm the diagnosis of NPC.

Contact endoscopy may make a significant contribution to dynamically monitoring the changes in epithelial cells of pre-malignant lesions and the population at high risk of oral -nasal-pharyngeal carcinoma. The use of contact endoscopy will also be helpful in repeated follow-up examination and will provide evaluation of the intervention test in the population at high risk with an objective method and index.

Our results support the potential for this tool to play a significant role in the clinical evaluation of oral lesions, real-time identification of tumor margins and monitoring of response to therapeutic treatment.

We find that microendoscopy can image oral mucosa with resolution comparable to histology without the need for tissue fixation, sectioning, or staining. Based on these results, we recommend that microendoscopy should be explored as a tool to improve early detection of oral cavity lesions, to provide real-time determination of mucosal tumor margins and to determine response to therapy.

CONCLUSION

Although, our study has demonstrated the potential of contact endoscopy to directly visualize the cellular morphology and help to direct the target site for biopsy, its main value as a screening procedure of oral lichen planus has not been elucidated. Further randomized, double-blinded studies of this technique are needed.

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