REVIEW ARTICLE

Advanced Diagnostic Aids in Detection of Oral Cancer

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ABSTRACT

Oral cancers are one of the most common cancers worldwide today. They are usually neglected by the common population when compared to systemic cancers such as the lung cancer, colon cancer etc. However, they also may be extremely fatal if left untreated even at a very initial stage of the lesion. Dental health care workers have a duty to detect benign and potentially malignant oral lesions such as oral cancer and are generally the best trained health care professionals in this field. Prompt referral to an appropriate specialist allows for the best management but, if this is not feasible, the dental practitioner should take the biopsy which should be sent to an oral/head and neck pathologist for histological evaluation. The purpose of this review article is to discuss the various advanced diagnostic aids in the diagnosis of oral cancer.

KEYWORDS: Diagnostic Techniques, Early Diagnosis, Oral Cancer

INTRODUCTION

In our oral cavity, oral cancer is a life threatening disease. It is a part of group of head and neck cancer which may arise as a primary lesion in any part of the oral cavity or oropharynx by metastasis from a distant site of origin. Oral cancer most commonly involves the tongue, floor of the mouth, buccal mucosa, gingiva and lips.[1] Approximately 94% of all oral malignancies are Squamous cell carcinoma (SCC). The annual incidence and mortality rates vary between different races, genders, and age groups. In the United States this is 7.7 per 100,000. Persons with oral SCC almost have been aware of an alteration in that site for 4–8 months before seeking professional help. There is minimal pain during the early growth phase and this may explain the delay in seeking professional care .If the health care professional does not have a high index of suspicion, additional several weeks or months may elapse before a biopsy is performed.[2]

It is expected that early diagnosis of premalignant lesion (PML) can reduce mortality. Early diagnosis of OSCC can speed proceeding to treatment and can improve the prognosis. This requires patients to seek an oral and dental examination at an early stage. Conventional oral examination (COE) is the standard method of revealing PML and OSCC, confirming the clinical suspicion by biopsy and histopathological examination. Histopathology

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has for many years been the gold standard in the diagnosis of OSCC; however, it is a rather slow process, requiring several days to fix, embed and stain the biopsy specimen before results can be available. It is subject to interpretation of pathologists, and although it can detect cellular changes, it can only detect molecular changes if special techniques are employed.[3] The purpose of this review article is to discuss the various advanced diagnostic aids in the diagnosis of oral cancer.

LAB ON A CHIP

Microfuidics technology- also referred to as lab-on-a-chip or micro-total-analysis systems (TAS)- is the adaptation, miniaturization, integration and automation of analytical laboratory procedures into a single device or "chip". Microfluidics is often regarded as the chemistry or biotechnology equivalent of the silicon integrated silicon chip that has revolutionized electronics, computers and communications. Microfluidics are by definition suited for handling living cells (whose typical diameter is a few micrometers) in a three-dimensional, biologically relevant environment. This microfluidic chip accepts saliva sample, can be operated by minimally trained personnel, and can provide a diagnostic answer in an automated and timely fashion. The detection of oral pre-cancer (dysplastic) and cancer cells within the chip will take advantage of membrane-associated cell proteins that are singularly expressed on cell cancer cells. The measured profile is compared with archived gene transcription profiles to determine the cancer type and stage.[2]

VITAL TISSUE STAINING: TOLUDINE BLUE STAINING & LUGOL'S IODINE

Oral carcinoma in situ and early invasive oral carcinoma shows affinity for toluidine blue dye. Lugol's iodine and toluidine blue have been used together in the detection of early carcinomas and other oral lesions. Toluidine blue is an acidophilic meta chromatic dye which selectively stains acidic tissue components, thus staining DNA and RNA. As it binds to nucleic acids (DNA or RNA), it helps in better visualization of high risk areas especially with rapid cell proliferation of OSCC and premalignant lesions. It stains mitochondrial DNA, cells with greater than normal DNA content or altered DNA seen in dysplastic and malignant cells. Lugol's solution is used for delineation of the malignant change which produces a brown black stain when the iodine reacts with the glycogen content. The use of toluidine blue and Lugol's iodine serves as a useful adjunct in the diagnosis of patients who are at risk and for selecting the site for biopsy with wide field cancers prior to treatment.[1]

BRUSH CYTOLOGY

Brush cytology (Oral CDX), developed in 1999 and has become popular in dental practice today. In the past decades, adjunctive technique has facilitates the early detection of oral premalignant and malignant lesions (OPML). In that context, Oral CDx is useful in the assessment of dysplastic changes in various suspected lesions especially in oral cancer. As majority of oral cancers are squamous cell carcinomas, Cytological study of oral cells is a relatively inexpensive, simple, noninvasive and also risk-free technique which is well accepted by the patient and medical practitioner today. The oral cells can be obtained by the use of a cytobrush. With brush cytology, sensitivity for detecting oral epithelial dysplasia or Oral squamous cell carcinoma is high. But, the technique has attracted lots of controversies and more incidences of false negative results with this technique has been encountered.[1]

OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (OCT) was first reported by Fujimoto et al. in 1991. OCT has been widely used in numerous clinical applications, including gastroenterology, ophthalmology, dermatology, and dentistry. OCT is a non-invasive, non-radiative optical diagnostic tool based on interferometers. Optical coherence tomography (OCT) has been proved to be a useful technique for oral disease diagnosis. In particular, based on the scanning images of a swept-source OCT system, a few effective diagnosis indicators for oral cancer and pre-cancer have been identified. These indicators include the EP layer thickness and the standard deviation (SD) of OCT signal intensity. In an abnormal oral EP containing dysplastic cells, the cell size, shape, nucleus size, and arrangement become more randomly distributed, when compared with healthy oral epithelium (EP). In this situation, light scattering becomes stronger and its spatial distribution becomes more strongly fluctuated.[2]

BIOMARKERS

Since the introduction of molecular techniques such as examination for abnormal protein expression, including tumor suppressor genes (TSGs) and other genetic changes, molecular markers have revealed neoplastic changes in PML (and furthermore may predict involvement of tumor resection margins and lymph nodes, and prognosis). The most predictive of the molecular markers thus far available and assessed in OSCC development include the TSG p53 protein expression, chromosomal polysomy (DNA ploidy), and changes (termed loss of heterozygozity; LOH) in chromosomes 3p or 9p (probably due to changes in the TSG p16). The use of such biomarkers as adjuncts to routine histopathological examination may help prognostication and effective management of PMLs but their routine use is still hampered by the cost and complexity of the tests, the lack of facilities in some laboratories, and limited outcome studies to date. More readily available markers, such as those of cell proliferation (Ki-67 antigen) and apoptosis (Bax, Bcl-2), may also play a diagnostic role: apoptotic Bcl-2 expression decreases significantly in dysplastic and early invasive lesions and then increases almost to normal tissue level in consequent stages while Ki-67 expression increases sharply in initial stages of OSCC, but significantly decreases in later stages.[3]

DNA PLOIDY

DNA ploidy is the measurement of nuclear DNA content. This may provide a surrogate measure of gross genetic damage and this could act as a surrogate for individual molecular markers. Normally, a non-dividing somatic cell contains a diploid amount of DNA in 23 pairs or 46 chromosomes. Just before cell division, the DNA is doubled and in mitosis; the 23 pairs of chromosomes are evenly distributed to two daughter cells. In somatic cells, if a doubling of the DNA during S-phase occurs without a subsequent cell division, the nucleus will then contain quadruples of the DNA, making the cell tetraploid. Multiple copies of DNA in excess of diploidy are termed polyploidy. If the chromosomes are not uniformly distributed to the daughter cells or if parts of chromosomes become detached, the chromosomal segregation during mitosis is termed unbalanced, a situation termed aneuploidy and commonly observed in many cancers.[3]

CHEMILUMINESCENCE: VIZILITE

This imaging device has been approved for use in the United States by the Food and Drug Administration since November 2001. It

involves the use of a hand-held, single-use, disposable chemiluminescent light stick that emits light at 430, 540 and 580 nm wavelengths. The use of the light stick is intended to improve the visual distinction between normal mucosa and oral white lesions. Normal epithelium will absorb light and appear dark whereas hyper keratinized or dysplastic lesions appear white. The difference in color could be related to altered epithelial thickness, or to the higher density of nuclear content and mitochondrial matrix that preferentially reflect light in the pathological tissues.[4]

VELSCOPE SYSTEM

The use of tissue autofluorescence in the screening and diagnosis of precancerous lesions in the lung, uterine cervix and skin has been well documented. This approach is already in clinical use in the lung, and its mechanism of action and interaction of tissue auto fluorescence has been well described in the cervix. Using the tissue autofluorescence concept for diagnosis of dysplastic lesions in the oral cavity hinges on the changes in the structure and metabolism of the epithelium and the subepithelial stroma when interacting with light. Specifically, loss of autofluorescence in dysplastic and cancerous tissue is believed to reflect a complex mixture of alterations to intrinsic tissue fluorophore distribution, due to tissue remodeling such as the breakdown of the collagen matrix and elastin composition as well as alterations to metabolism such as the decrease in flavin adenine dinucleotide concentration, and increase the reduction form of nicotinamide adenine dinucleotide associated with progression of the disease.[4]

SALIVA AS A DIAGNOSTIC TOOL

Saliva from patients has been used in a novel way to provide molecular biomarkers for oral cancer detection. Saliva is a mirror of the body, reflecting virtually the entire spectrum of normal and disease states and its use as a diagnostic fluid meets the demands for an inexpensive, non-invasive and accessible diagnostic tool. Discovery of analytes in saliva of normal and diseased subjects suggests a very promising function of saliva as a local and systematic diagnostic tool. The ability to analyze saliva to monitor health and disease is a highly desirable goal for oral health promotion and research. So far, saliva has been used to detect caries risk, periodontitis, oral cancer, breast cancer, salivary gland diseases and systemic disorders such as human immunodefficiency virus and hepatitis C virus. However, due to lack of knowledge of disease markers and an overall low concentration of these markers in saliva when compared to serum, the diagnostic value of saliva has not been fully realized.[4]

CONCLUSION

Unfortunately, no technique or technology to date has provided definitive evidence to suggest that it improves the sensitivity or specificity of oral cancer screening beyond clinical oral examination. Further detailed investigations to estimate the sensitivity, specificity, positive and negative predictive values for each of these adjunctive tests against standard pathology reporting (cancer or dysplasia) will allow us to judge the accuracy of these chair side or laboratory tests in detecting cancer or oral pre-malignant lesions.[5]

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