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Review Article

Advanced diagnostic techniques in oral pathology: A review

Ayeda Jehan[1], Rubeena Anjum[1], Pradakhshana Vijay[1], Priyanka Singh[2], Wajiha Khanam[1]*, Ruchika Raj[1]

[1]*Dept. of Oral Pathology & Microbiology, Indira Gandhi Govt. Dental College, Jammu, Jammu & Kashmir, India*
[2]*Dept. of Oral Pathology & Microbiology, Faculty of Dental Sciences, King George's Medical University, Lucknow, Uttar Pradesh, India*

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ABSTRACT

Oral cancer is one of the most common cancers in the world today. Oral potentially malignant disorders (OPMDs) typically occur before oral cancer, although it can be difficult to predict if an OPMD will progress to cancer. Oral cancer typically receives less public attention than systemic cancers such as lung cancer, colon cancer, etc. Even with an early diagnosis, these lesions may be fatal if left untreated. The prognosis for effective treatment is improved by early diagnosis. The diagnostic tools available to identify oral cancer in its early stages have advanced in a number of ways. This study aims to dissect the cutting-edge methods for early detection of oral cancer.

1. Introduction

Tobacco, alcohol, and betel use are the primary risk factors for oral squamous cell carcinomas (OSCC), the majority of oral malignancies, as well as many other potentially malignant lesions (PML).[1,2] Early PML diagnosis is anticipated to lower mortality.[3,4] Prognosis can be improved and treatment can begin more quickly in cases of early OSCC diagnosis.[5] Currently, the gold standard for identifying potentially malignant diseases (PMDs) and oral squamous cell carcinoma (OSCC) is routine oral examination (visual and tactile assessment of accessible oral structures) combined with tissue sampling. Nevertheless, there are several drawbacks to this approach as well, such as sample bias, which may lead to an incorrect or underdiagnosed diagnosis, particularly in the case of multifocal lesions.[6] Hence, the search for noninvasive, quick, and affordable screening techniques with sufficient sensitivity and specificity for the early detection of oral cancer is urgently needed. Thus, the various diagnostic methods used to identify precancerous and cancerous lesions are as follows:

1. Conventional oral examination
2. Vital tissue staining
3. Histopathological methods
   (a) Exfoliative cytology
   (b) Oral brush biopsy
   (c) Liquid based cytology
   (d) Fine Needle Aspiration Cytology (FNAC)
   (e) Biopsy and histopathology
   (f) Electron microscopy
   (g) Histochemistry
4. Molecular methods
   (a) Hybridization techniques.
   (b) Polymerase Chain Reaction (PCR)
   (c) Microarray

* *Corresponding author*.
E-mail address: wajiha96khanam@gmail.com (W. Khanam).

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(d) Flow Cytometry
(e) Immunohistochemistry (IHC)-Tumour markers
(f) Laser Capture Micro dissection (LCM)

5. Optical techniques

(a) Fluorescence spectroscopy
(b) Vizilite
(c) VELscope [7]

6. Other methods

2. Conventional Oral Examination

Under typical incandescent light, the oral cavity is the site of the customary examination. For a very long time, it has been the accepted procedure for screening for oral cancer. Although it works wonders for some skin conditions, there is still debate on its applicability to oral cancer screening. [8,9]

3. Vital Tissue Staining

In addition to toluidine blue, acetic acid, methylene blue, and iodine have also been tried as staining techniques. Acidophilic dye toluidine blue, which belongs to the thiazine group, is used to stain acidic cell tissue elements like DNA and RNA. It attaches itself to DNA by stacking, aggregating, or intercalation. The quantity of DNA determines the degree of binding. Loss of cell cohesion, accelerated mitosis, more nucleic acids, and bigger intracellular channels that improve dye penetration are all thought to contribute to the uptake of dye by dysplastic lesions and carcinomas. [10]

4. Exfoliative Cytology

In order to exfoliate deeper cells as well as superficial cells, which are scraped off and examined under a microscope, epithelial cells beneath neoplasms must lose their cohesiveness, according to the fundamental principle of exfoliative cytology. [11] Its non-invasiveness, speed, simplicity, and suitability for patients with systemic disorders are its advantages. Cytology is an addition to surgical biopsy, not a replacement for it. [11,12]

5. Oral Brush Biopsy

A straightforward, non-invasive chairside procedure called brush biopsy takes a full thickness sample of the lesion. Until precise bleeding is clinically identified, the brush is applied to the lesion and rotated. After being collected, the cellular material is put on a slide, coated, dyed, and then examined using a computer. [7]

6. Liquid-Based Cytology

One of the newest advancements in screening technologies is liquid-based cytology. Using a brush-like tool, samples are gathered, dipped in a vial of liquid preservative, and then brought to the laboratory where they are cleared of any obscuring substances, mucus, and blood before being centrifuged using a standard centrifugation technique to extract the cells. After discarding the supernatant, the resulting film is combined with a cell base solution and placed onto a sanitized slide. [13,14]

7. Fine Needle Aspiration Cytology

For oral squamous cell carcinoma, FNAC is a valid diagnostic tool; however, its applicability in cases of oral leukoplakia is restricted. [15] Because both benign and malignant salivary gland neoplasms share overlapping morphologic characteristics, FNA in salivary gland lesions is one of the most challenging areas of cytopathology. Additionally, different histological patterns within the same tumor may reveal different characteristics. [16]

8. Biopsy and Histopathology

Biopsy and histological inspection continue to be the gold standard for cancer diagnosis, despite the abundance of supplements available. [14,17] While clinical supplements aid in lesion visualization, only histological testing can determine the extent, depth, and degree of the lesion. [7]

9. Molecular Methods

Fluorescent in situ hybridization (FISH), chain reaction (PCR), microarray, flow cytometry, immunohistochemistry (IHC), tumour markers, and laser capture microdissection (LCM) are among the many molecular techniques that are available. [18] These methods can be applied to immunophenotyping, chromosomal mapping, prognostic, genomic, and proteomic tumor marker validation, generation of new markers, biology diagnosis, cytogenetic cancer diagnosis, and DNA ploidy determination. [7,18] The accuracy and usefulness of diagnostic testing have increased with the use of the PCR method. The main issue is that it is still prone to amplification artifacts and contamination, which could make data interpretation more difficult. [19] In situ hybridization (ISH) can be produced by combining molecular biology techniques with measures of gene expression in tissues and cells. In this manner, it is easy to identify specific cells using RNA and DNA. [20]

10. Fluorescence Spectroscopy

The apparent benefits of being able to diagnose disease without having to remove a tissue sample reduce patient trauma and have financial ramifications. Optical spectroscopy systems are valued for their ability to provide tissue diagnostics quickly, in real-time, non-invasively, and in situ. [21–23] The three primary spectroscopic methods now employed to identify malignancies and oral

dysplasia are fluorescence, Raman and elastic scattering (ESS).[22] An emerging method called ESS produces a wavelength-dependent spectrum that shows morphological and structural changes in tissues. It provides information about the tissue's absorptive and scattering characteristics throughout a broad spectrum of wavelengths.[7]

11. Vizilite

Studies have demonstrated that Vizilite enhances conventional visual evaluation. At 430, 540, and 580 nm, a single-use, disposable chemiluminescent light stick emits light. This may be handled with one hand. Normal epithelium (EP) absorbs light and appears black, but hyperkeratinized or dysplastic tumors reflect light and appear white.[17] To detect oral cancer early, observe any changes with a chemiluminescent light (like Vizilite) and rinse with diluted acetic acid.[24]

12. Velscope

It is a portable optical device that allows for direct observation of oral autofluorescence. Medical experts can now utilize it as a helpful diagnostic tool to identify oral sickness early on. It has recently been available. It has been beneficial in the detection and prevention of several cancers, including as those of the skin, cervix, lung, and oral cavity. The principal justification for employing tissue autofluorescence in the identification of dysplastic lesions within the oral cavity is based on the ways in which light modifies the structure and uptake of both the epithelium and the subepithelial stroma.[25]

13. Saliva-Based Oral Cancer Diagnostics

The use of saliva in the detection of OSCC is relatively new. Oral fluid, sometimes known as saliva, is a widely accessible, non-invasive, and highly useful diagnostic tool. There's a chance that saliva transcriptome-based diagnostics will be utilized in the future to identify oral cancer.[26] In addition to abnormally high levels of O6-methyl guanine-DNA methyltransferase, death-related protein kinase, and tumor suppressor gene (TSG) p16, patients with head and neck conditions also had abnormally high levels of Capnocytophaga gingivalis, Prevotella melaninogenica, and Streptococcus mitis in their saliva. However, there is currently insufficient data to back up the idea that sound could be a reliable diagnostic indicator.[27]

14. Dna Ploidy and Quantification of Nuclear DNA Content

The quantity of DNA copies in a cell's nucleus, or DNA ploidy, can be used as a stand-in for the degree of genetic damage. The separation of chromosomal segments or the unequal distribution of chromosomes among daughter cells during mitosis are the main causes of aneuploidy in many malignancies. DNA image cytometry is a sensitive method that doesn't require tissue biopsy for cancer detection.[28]

15. Serum Profiling

In patients with oral cancer, serum profiling has revealed variations in the amounts of a few minerals, antigens, and immune complexes. According to a study, people with oral cancer had considerably lower levels of iron and selenium and greater amounts of copper. Its low diagnostic sensitivity and specificity raise doubts about its dependability as a diagnostic tool.[29,30]

16. Di-electrophoresis

It can be utilized as a possible tool for the early identification of oral cancer because it is a non-invasive method to measure the conductivity, permittivity of cellular cytoplasm and membrane, and other electrophysiological characteristics.[31]

17. Molecular Imaging in Adjunct with Ct, Mri and Pet

When used in conjunction with CT, MRI, and PET scans, molecular imaging has the potential to improve cancer detection and staging by highlighting the distinct functional characteristics of cancerous cells. Molecular imaging applications have demonstrated in a number of recent investigations that they can reveal characteristics of carcinogenesis at much earlier stages.[31]

18. Identafi 3000

In conjunction with traditional anatomical imaging, this technique makes use of fluorescence, fiber optics, and confocal microscopy to precisely map and highlight the lesion in the screened region (Identafi 3000, Dental EZ, Malvern, PA, USA). Because it is small, it can easily reach every tissue in your mouth. Changes in angiogenesis can be observed by flashing a certain green-amber light on the tissue, much like a VELscope.[32]

19. Conclusion

The field of histopathology anticipates that diagnostic macroscopic and microscopic will advance in tandem with molecular pathology, not in opposition to it. With the primary goal of treating PMLs and OSCCS as soon as possible, it is clearer what function these cutting-edge, futuristic diagnostic clinical tools serve. Early detection can prevent the lesions from becoming cancerous, which can result in the early creation of treatment tailored to each patient. The importance of these state-of-the-art, forward-thinking diagnostic clinical techniques is further highlighted by the urgent need for early PML and OSCC identification and treatment.

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21. Conflict of Interest

None.

References

1. Waldron CA, Shafer WG. Leukoplakia revisited. A clinicopathologic study 3256 oral leukoplakias. *Cancer*. 1975;36(4):1386–92.
2. Wright JM. Oral precancerous lesions and conditions. *Semin Dermatol*. 1994;13:125–31.
3. Sankaranarayanan R. Screening for cervical and oral cancers in India is feasible and effective. *Natl Med J India*. 2005;18(6):281–4.
4. Sankaranarayanan R, Ramadas K, Thomas G, Muwonge R, Thara S, Mathew B, et al. Trivandrum oral cancer screening study group. Effect of screening on oral cancer mortality in Kerala, India: A cluster-randomised controlled trial. *Lancet*. 2005;365(9475):1927–33.
5. Massano J, Regateiro FS, Januario G, Ferreira A. Oral squamous cell carcinoma: Review of prognostic and predictive factors. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;102(1):67–76.
6. Yang EC, Tan MT, Schwarz RA, Richards-Kortum RR, Gillenwater AM, Vigneswaran N. Noninvasive diagnostic adjuncts for the evaluation of potentially premalignant oral epithelial lesions: current limitations and future directions . *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2018;125(6):670–81.
7. Padmanabhan G, Narayan M, Krishnan R. Recent diagnostic aids in oral squamous cell carcinoma - a detailed review. *Oral Oncol Rep*. 2024;10:100323.
8. Lingen MW, Kalmar JR, Karrison T, Speight PM. Critical evaluation of diagnostic aids for the detection of oral cancer. *Oral Oncol*. 2008;44(1):110–22.
9. Patton LL. The effectiveness of community-based visual screening and utility of adjunctive diagnostic aids in the early detection of oral cancer. *Oral Oncol*. 2003;39(7):708–23.
10. Martin IC, Kerawala CJ, Reed M. The application of toluidine blue as a diagnostic adjunct in the detection of epithelial dysplasia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998;85(4):444–6.
11. Sivapathasundharam B, Kalasagar M. Yet another article on exfoliative cytology. *J Oral Maxillofac Pathol*. 2004;8(2):54–54.
12. Ogden GR, Cowpe JG, Wight AJ. Oral exfoliative cytology: review of methods of assessment. *J Oral Pathol Med*. 1997;26(5):201–5.
13. Kujan O, Desai M, Sargent A, Bailey A, Turner A, Sloan P. Potential applications of oral brush cytology with liquid-based technology: results from a cohort of normal oral mucosa. *Oral Oncol*. 2006;42(8):810–8.
14. Navone R, Pentenero M, Rostan I, Burlo P, Marsico A, Broccoletti R, et al. Oral potentially malignant lesions: first-level micro-histological diagnosis from tissue fragments sampled in liquid-based diagnostic cytology. *J Oral Pathol Med*. 2008;37(6):358–63.
15. Seetharam SS, Ramachandran CR. Fine needle aspiration cytology as a diagnostic test for oral squamous cell carcinoma. *Oral Dis*. 1998;4(3):180–6.
16. Rajwanshi A, Gupta K, Gupta N, Shukla R, Srinivasan R, Nijhawan R, et al. Fine-needle aspiration cytology of salivary glands: diagnostic pitfalls–revisited. *Diagn Cytopathol*. 2006;34(8):580–4.
17. Epstein JB, Zhang L, Rosin M. Advances in the diagnosis of oral premalignant and malignant lesions. *J Can Dent Assoc*. 2002;68(10):617–21.
18. Jordan RC, Daniels TE, Greenspan JS, Regezi JA. Advanced diagnostic methods in oral and maxillofacial pathology. Part I: molecular methods. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2001;92(6):650–69.
19. Vaidya MM, Borges AM, Pradhan SA, Rajpal RM, Bhisey AN. Altered keratin expression in buccal mucosal squamous cell carcinoma. *J Oral Pathol Med*. 1989;18:282–6.
20. O'Leary JJ, Engels K, Dada MA. The polymerase chain reaction in pathology. *J Clin Pathol*. 1997;50:805–10.
21. Lingen MW, Kalmar JR, Karrison T, Speight PM. Critical evaluation of diagnostic aids for the detection of oral cancer. *Oral Oncol*. 2008;44(1):10–22.
22. Swinson B, Jerjes W, El-Maaytah M, Norris P, Hopper C. Optical techniques in diagnosis of head and neck malignancy. *Oral Oncol*. 2006;42(3):221–8.
23. Mahadevan-Jansen A, Richards-Kortum RR. Raman spectroscopy for the detection of cancers and precancers. *J Biomed Opt*. 1996;1(1):31–70.
24. Abdul NS. Role of Advanced Diagnostic Aids in the Detection of Potentially Malignant Disorders and Oral Cancer at an Early Stage. Cureus. *Cureus*. 2023;15(1):e34113.
25. García-Pola M, Pons-Fuster E, Suárez-Fernández C, Seoane-Romero J, Romero-Méndez A, López-Jornet P. Role of artificial intelligence in the early diagnosis of oral cancer. A scoping review. *Cancers (Basel)*. 2021;13(18):4600.
26. Li Y, John MS, Zhou X, Kim Y, Sinha U, Jordan RCK, et al. Salivary transcriptome diagnostics for oral cancer detection. *Clin Cancer Res*. 2004;10(24):8442–50.
27. Scully C, Bagan JV, Hopper C, Epstein JB. Oral cancer: current and future diagnostic techniques. *Am J Dent*. 2008;21(4):199–209.
28. Maraki D, Becker J, Boecking A. Cytologic and DNA-cytometric very early diagnosis of oral cancer. *J Oral Pathol Med*. 2004;33(7):398–404.
29. Khana SS, Karjodkar FR. Circulating immune complexes and trace elements (copper, iron, selenium) as markers. *Head Face Med*. 2006;2:33.
30. Faria PCB, Servino-Sena AA, Nascimento R, Carvalho WJ, Loyola AM, Silva SJ, et al. Expression of annexin A1 mRNA in peripheral blood from oral squamous cell carcinoma patients. *Oral Oncol*. 2010;46(1):25–30.
31. Broche LM, Bhadal N, Lewis MP, Porter S, Hughes MP, Labeed FH. Early detection of oral cancer- is dielectrophoresis is the answer? *Oral Oncol*. 2007;43(2):199–203.
32. Sujir N, Ahmed J, Pai K, Denny C, Shenoy N. Challenges in early diagnosis of oral cancer: cases series. *Acta Stomatol Croat*. 2019;53(2):174–80.

Author biography

Ayeda Jehan, 1st Year Post Graduate Student

Rubeena Anjum, Professor and Head

Pradakhshana Vijay, Lecturer

Priyanka Singh, Additional Professor

Wajiha Khanam, 1st Year Post Graduate Student

Ruchika Raj, 2nd Year Post Graduate Student

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