Oral cancer and early detection

Diagnostic Aids

Diagnostic Aids for Early detection

- Early detection of potentially malignant and malignant lesions is a continuing goal.

- Patient history, thorough head and neck and intraoral examinations, is a prerequisite.

- The definitive test for diagnosis remains tissue biopsy.

- Several aids to the oral examination have been suggested in the past, including:
  light technologies,
- vital tissue staining using toluidine blue (TB),
- and computer-assisted cytology of oral brush biopsy specimens.
- Additional markers based on blood or saliva samples are also under investigation.

Toluidine Blue

- Vital staining with TB may be used as an adjunctive aid in assessing potentially malignant oral mucosal lesions.

- TB is a metachromatic dye, which has an affinity to bind with DNA.
- TB staining has been correlated with LOH profiles in tissue biopsies.
- TB can be applied directly to suspicious lesions or used as an oral rinse.
- The assessment of dye uptake depends on clinical judgment and experience
- Positive retention of TB (particularly in areas of leukoplakia, erythroplakia, and uptake in a peripheral pattern of an ulcer) may indicate the need for biopsy or assist in identifying the site of biopsy.

- **False-positive** dye retention may occur in inflammatory and ulcerative lesions, but **false-negative** retention is uncommon.

- A return appointment in 14 days, providing time for inflammatory lesions to improve, may lead to a decrease in false-positive results.

- TB has been suggested as a **diagnostic tool** in potentially malignant oral lesions at risk of progressing to squamous cell cancer, where it may provide guidance for the selection for the biopsy site and accelerates the decision to biopsy.

- In postradiotherapy follow-up, the retention of TB may assist in distinguishing Non-healing ulcers and persistent or recurrent disease.

Visualization Adjunctive Tools

- **Chemiluminescent devices** generate **light based on chemical reactions**. The suspected area of mucosa appears **brighter**.

- Other products **generate fluorescent light using a LED source**, sometimes combined with **optical filtration of a viewfinder**, to enhance natural tissue fluorescence.
- When using the **fluorescence light**, the suspected area shows **loss of fluorescence, which appears dark.**

- **Oral cavity fluorescence**, using **blue light excitation**, is thought to represent the tissue structure, metabolic activity, presence of hemoglobin, vessel dilatation, and possibly inflammation.

- Localized modification in these factors may change the reflective features of the tissue.

- These products are promoted to assist the practitioner in discovering mucosal abnormalities, specifically oral potentially malignant disorders and evaluate margins of resection site.

- There is no consensus regarding the sensitivity and specificity of these devices, and their ability to detect early disease. Nonetheless, fluorescence has been shown to provide evidence on lesion margins in patients with known malignant lesions.
- There is an increasing interest in the use of confocal microscopy and optical coherent tomography systems to provide tissue diagnosis in real time, noninvasively, and in situ.

- Such diagnostic approach is available in dermatology and anticipated to be developed for oral mucosal application in the future.

- Other imaging modalities are being studied due to the need for improved detection and to assist in diagnosis and treatment.

Cytology

- Cytology of the oral mucosa is used to assess cellular morphology. The introduction of a brush designed to sample the entire thickness of the oral epithelium renewed interest in cytology for oral disease.

Originally, the cytobrush was combined with a computer- assisted analysis of the cytologic sample, assessing the cell morphology and keratinization.

- The final diagnosis was made by a pathologist based on the standard histomorphologic criteria.

- Further developments in cytology include molecular evaluation of exfoliated cells for molecular markers of dysplasia or carcinoma to improve the diagnostic and prognostic value.

Molecular Analysis

- Molecular markers obtained from tissue specimens have been suggested to assist with detection and evaluation of cancerous lesions including c-erbB2, Ki67/Mcm2, Cyclin D1, p53, COX-1 and 2, telomerase, loss of 3p or 9p, 8p, 4q, 11q, 13q, 17p.
- Studies have also shown that biomarkers of OSCC are present in saliva

Imaging

- Routine radiology, computed tomography (CT), nuclear scintiscanning, magnetic resonance imaging, and ultrasonography can provide evidence of bone involvement or can indicate the extent of some soft tissue lesions.

- The selection of the appropriate imaging modality is dependent on the type and location of the suspected tumor.

- Positron emission therapy using the radiolabeled glucose analog 18fluorodeoxyglucose offers a functional imaging approach for the entire body.
- Positron emission tomography (PET) is a type of nuclear medicine procedure that measures metabolic activity of the cells of body tissues.

- PET is actually a combination of nuclear medicine and biochemical analysis.

- Used mostly in patients with brain or heart conditions and cancer,
- PET helps to visualize the biochemical changes taking place in the body, such as the metabolism.

- PET differs from other nuclear medicine examinations in that PET detects **metabolism** within body tissues, whereas other types of nuclear medicine examinations detect the amount of a **radioactive substance** collected in body tissue in a certain location to examine the tissue's function.
- PET is most often used by oncologists, neurologists, neurosurgeons, cardiologists
- PET may also be used in conjunction with other diagnostic tests, such as computed tomography (CT) or magnetic resonance imaging (MRI) to provide more definitive information about malignant (cancerous) tumors and other lesions.

Acquisition of a Tissue Specimen

- In addition to standard surgical biopsy techniques, tissue can be acquired for histopathology by using fine-needle aspiration (FNA) or core needle biopsy (CNB).

- Open biopsy of enlarged lymph nodes is not recommended; in such cases, FNA biopsy should be considered.

- FNA/CNB also may aid in the evaluation of suspicious masses in other areas of the head and neck, including masses that involve salivary glands, tongue, and palate, or when there is contraindication for conventional biopsy (e.g., thrombocytopenia).
- Ultrasound may assist in guiding FNA/CNB.

Treatment

- The principal objective of treatment is to cure the patient of cancer.
- The choice of treatment depends on cell type and degree of differentiation, the site and size of the primary lesion, lymph node status, the presence of local bone involvement, the ability to achieve adequate surgical margins, and the presence or absence of metastases.
- Treatment decisions are also impacted by appraisal of the ability to preserve oropharyngeal function, including speech, swallowing, and esthetics, as well as the medical and mental status of the patient.

❑Surgery

Surgery is indicated for
(1) early or localized oral cancer,
(2)tumors involving bone, and when the side effects of surgery are expected to be less significant than those associated with radiation,
(3) tumors that lack sensitivity to radiation, and
(4) recurrent tumor in areas that have previously received radiotherapy.

Surgery also may be used in palliative cases to reduce the bulk of the tumor and to promote drainage from a blocked cavity (e.g., antrum).

- Surgical excision of dysplastic and malignant lesions can be accomplished with laser therapy.
- Such therapy for these lesions is generally well tolerated and usually decreases the period of hospitalization and may have similar outcomes as traditional surgical interventions.

- However, laser therapy has the disadvantage of limiting the assessment of the margins for histopathologic confirmation.

- New surgical approaches and new approaches to reconstruction, such as vascularized flaps, microvascular reconstruction, and neurologic anastomoses of free grafts.
- Reconstruction with the use of osseointegrated implants offers the ability to provide stable prostheses and enhanced esthetic and functional results.
- The ability to place implants in irradiated bone has increased options for rehabilitation

Radiation Therapy

- Radiation therapy may be administered with intent to cure, as a single modality, as part of a combined radiation surgery and/or chemotherapy management, or for palliation.
- Radiotherapy with intent to cure causes early and late toxicities.
- In palliative care, radiation may provide symptomatic relief from pain, bleeding, ulceration, and oropharyngeal obstruction.
- Hyperfractionation of radiation (usually twice daily dosing) is one of the strategies to increase intensity of treatment to increase tumoricidal effects, which results in more severe acute effects.

- High-dose re-irradiation is offered in some centers as save treatment and may be considered in case of recurrent or second primary head and neck cancer, particularly when salvage surgery is not feasible.

- Radiation kills cells by interaction with water molecules in the cells, producing charged molecules that interact with biochemical processes in the cells and by causing direct damage to DNA
- The affected cells may die or remain incapable of division.
- Due to a greater potential for cell repair in normal tissue than in malignant cells and a greater susceptibility to radiation due to the higher growth fraction of cancer cells, a differential effect is achieved.
- To achieve therapeutic effects, radiation therapy is delivered in daily fractions for a planned number of days.

The biologic effect of radiation depends on the dose per fraction, the number of fractions per day, the total treatment time, the total dose of radiation, and the radiation used (electron, neutron, proton).

Methods for representing the factors of dose, fraction size, and time of radiation with a single calculation using the time-dose fraction (TDF) and the nominal standard dose (NSD) calculations have been described.

- Radiation therapy has the advantage of treating the disease in situ and avoiding the need for the removal of tissue and may be the treatment of

choice for many T1 and T2 tumors, particularly in the base of the tongue and oropharynx.

- Radiation may be administered to a localized lesion by using implant techniques (brachytherapy) or to a region of the head and neck by using external beam radiation.

Cancer Treatment Planning

The radiation treatment plan is determined by the tumor site and size, relation to vital structures, the volume to be radiated, radiation technology available, the number of treatment fractions, the total number of days of treatment, and the tolerance of the patient.

Chemotherapy Cytotoxic Chemotherapy

- Chemotherapy may be used as induction therapy prior to local therapies, concurrent chemoradiotherapy (CCRT), and adjuvant chemotherapy after local treatment.
- The common chemotherapy protocols are listed in Table (8-6).
- The objective of induction chemotherapy is to promote initial tumor reduction and to provide early treatment of micrometastases due to the recognition that local control.

The principal agents that have been studied alone or in combination in head and neck cancer are taxol and derivatives, platinum derivatives (cisplatin and carboplatin), 5-fluorouracil, and hydroxyurea, although hydroxyurea is rarely used in current protocols.

Photodynamic Therapy

- Photodynamic therapy applies light over a tissue that initially absorbed exogenous sensitizer.

- The sensitizing agent may be delivered systemically or topically and then after it selectively accumulates in target tissue.

- The subsequent light delivery to the target tissue results in cellular destruction.

- Due to the focused cellular destruction, the complications and disfigurement associated with this treatment are relatively small.

- Although photodynamic therapy in oral cancer has some encouraging preliminary results, it is not accepted routine treatment.

Gene Therapy

- Gene therapy is being studied with the objective of reversing dysplasia in oral epithelial lesions.

- The modalities evaluated include suicide gene therapy, immunotherapy, oncolytic virus therapy, inhibition of tumor angiogenesis, gene deletion therapy, and antisense RNA.

- Considering the high rate of mutation in p53 in oral cancer, gene therapy focused on p53 gene, mostly with adenoviral vectors, shows promise.

- Additional target genes and vectors are currently being studied.

- None of these approaches have reached conventional clinic care settings

Immunotherapy

- Immunotherapy offers the potential for additional approaches to management, alone or in combination with other therapies.

- Clinical practice guidelines for management of malignant melanoma and other cancers are forthcoming.

- **Keytruda** May be used with the chemotherapy medicines fluorouracil and a platinum as first treatment when head and neck cancer has spread or returned and cannot be removed by surgery.

- Based on an analysis of a gene expression profile in matched tumor and normal fibroblast cell lines, a number of proteins have been detected that might be potential targets for immunotherapy in individuals with head and neck cancer.

- Cell lines studies and animal models support the introduction of immunotherapy for treatment of head and neck cancer.