Oral cancer

Dr Swati Gupta
Reader
Oral Medicine and Radiology

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A neoplasm is an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli that evoked the change.
Oral cancer – King of the jungle

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Oral cancer is the eleventh most common cancer in the world with an estimated 267,000 cases and 128,000 deaths in around 2000, two-third of which occurs in developing countries.

Six million people die due to cancer every year.

Although representing 2-4% of the malignancies in the West, squamous cell carcinoma accounts for almost 40% of all cancers in the Indian subcontinent.

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In India, it is the most common cancer among males and 4th most common cancer amongst females.

The age standardized incidence rate of oral cancer is 12.6/100,000 population.

Despite numerous advances in the treatment, the 5-year survival has remained approximately 50% for the last 50 years.

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Tobacco contains potent carcinogens, including nitrosamines (nicotine), polycyclic aromatic hydrocarbons, nitrosodiethanolamine, nitrosopropoline, and polonium.

Tobacco smoke contains carbon monoxide, thiocyanate, hydrogen cyanide, nicotine, and metabolites of these constituents.

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✓ Synergistic effect
✓ denture use, denture irritation, irregular teeth or restorations, and chronic cheek-biting habits.
✓ lip cancer, sun exposure, fair skin, tendency to burn, pipe smoking, and alcohol.
✓ Conditions like plummer vinson syn, immunosuppressed conditions, and malignancies secondary to leukemia, lymphoma.
Pathogenesis

Molecular Model of Dysplasia and Carcinogenesis

- Loss of Heterozygosity (LOH)
- Normal
- Hyperplasia
- Dysplasia (Mild and Severe)
- Carcinoma-in-situ

Progression of Dysplasia

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Viruses in oral cancer

• Herpes simplex virus (HSV) has been shown to produce a number of mutations in cells.
• Neutralizing antibodies to HSV are present in the serum of patients with oral cancer at higher titers as compared to controls.
• “hit and run effect”
• HPV with anogenital cervical dysplasia, carcinoma in situ, invasive carcinoma, well established.
Tumour biology

- Onco gene amplification has been seen in oral carcinoma.
- Cytokines including epidermal, transforming growth factor relevant in scc.
- Cell surface markers are altered
- Carcinoembryonic antigens are elevated
- Decreased T cells
- Langerhans cells increased

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Prognosis
<table>
<thead>
<tr>
<th>(Size of Primary Tumor)</th>
<th>N (Cervical Lymph Node Metastases)</th>
<th>M (Distant Metastases)</th>
<th>Staging</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1s: carcinoma in situ</td>
<td>N0: no node involvement detected</td>
<td>M0: no known metastases</td>
<td>Stage 1: T1 N0 M0</td>
</tr>
<tr>
<td>T1: tumor &lt; 2 cm</td>
<td>N1: single ipsilateral node &lt; 3 cm</td>
<td>M1: metastases present</td>
<td>Stage 2: T2 N0 M0</td>
</tr>
<tr>
<td>T2: tumor &gt; 2 cm and &lt; 4 cm</td>
<td>N2a: single ipsilateral node &lt; 6 cm</td>
<td></td>
<td>Stage 3: T3 N0 M0;</td>
</tr>
<tr>
<td>T3: tumor &gt; 4 cm</td>
<td>N2b: multiple ipsilateral nodes &gt; 3 cm and &lt; 6 cm</td>
<td></td>
<td>T1, T2, or T3 N1 M0</td>
</tr>
<tr>
<td>T4: tumor &gt; 4 cm with invasion of adjacent structures (ie, through cortical bone, muscles of tongue, maxillary sinus, and skin)</td>
<td>N2c: bilateral or contralateral lymph nodes &lt; 6 cm 3a: ipsilateral node &gt; 6 cm 3b: bilateral nodes &gt; 6 cm</td>
<td></td>
<td>Stage 4: T4 any N M0; any T N2 or N3 M0; any T or N, with M1</td>
</tr>
</tbody>
</table>

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CLINICAL FEATURES OF ORAL CANCER
• Displaced teeth
• Loosened teeth over a short period
• Foul smell
• Ulceration
• Induration or rolled borders
• Exposure of underlying bone
• Sensory or motor neural deficits
• Lymphadenopathy
• Weight loss
• Dysgeusia
• Dysphagia
• Dysphonia
• Hemorrhage
• Lack of normal healing after surgery
• Pain or rapid swelling with no cause
• Above 50 yrs

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Clinical appearances of oral cancer

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• carcinoma

• sarcoma

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• carcinoma

• sarcoma

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IMAGING

- routine radiology
- computed tomography (CT)
- nuclear scintiscanning
- magnetic resonance imaging (MRI)
- ultrasonography
Radioresistance in sarcomas compared to carcinomas

• Less Penetration power for bulky tumor masses, more tendency for metastases.

• Due to some molecular changes: P-glycoprotein expression, telomerase activity, angiogenesis, Tumor Suppressor p16 Mutation, Increased expression of Bcl-2, Bcl-xL, and XIAP, and hypoxia due to bulk of tumor (deep seated compared to carcinomas)

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• cytology
• Toluidine blue
• Computer assisted cytology of oral brush biopsy specimen
• Light based detection systems
• Scalpel biopsy[bios:life; opsis: vision]
• FNAC
• DNA Aneuploidy
• molecular analysis: AGNOR counts (Nucleolar organiser regions (NORs) are defined as nucleolar components containing a set of argyrophilic proteins, which are selectively stained by silver methods.)
Conventional Screening Tools for Oral Soft Tissues

- 2 x 2 Gauze
- Mouth Mirror
- Incandescent Light
- Magnification
- Human Eye
- Hands

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EXFOLIATIVE CYTOLOGY
Only Surface Cells Captured

Broom sweep limited to superficial cells

SPECIMEN

Superficial
Intermediate
Basal

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• Class 0: Inadequate specimen
• Class 1: No/abnormal or atypical cells
• Class 2: Atypical cytology but no evidence of malignancy
• Class 3: Cytology suggestive of but not conclusive for, malignancy
• Class 4: Cytology strongly suggestive of malignancy
• Class 5: Cytology conclusive for malignancy.
The OralCDx Test Kit

• Components of kits:
  – oral brush biopsy instrument
  – precoded glass slide and matching coded test requisition form
  – alcohol/carbowax fixative pouch
  – preaddressed container for submitting the contents

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The Brush Biopsy Instrument

- The brush is sterile
- One OralCDx test kit per oral lesion
- The brush was designed to penetrate to the basement membrane and thus achieve a complete transepithelial specimen
- Unlike cytology instruments which collect only superficial cells, the biopsy brush obtains cells from all three epithelial layers of the oral mucosa: superficial, intermediate and basal
BRUSH BIOPSY
Complete Transepithelial Tissue Sample

OralCDx Brush Biopsy Instrument

Superficial Intermediate Basal

SPECIMEN

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OralCDx Results

Classification

“inadequate”: re-test

“negative”: no cellular abnormalities

Abnormal Results:

“positive”: definitive cellular evidence of epithelial dysplasia or carcinoma

“atypical”: abnormal epithelial changes warranting further investigation

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Liquid-Brush Cytology

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Liquid-Brush Cytology

- Can Be Used to Test for the Presence of:
  - Cellular Abnormalities
  - Fungal Infections
  - Human Papilloma Virus (HPV)
  - DNA Abnormalities / Ploidy Analysis
    - Measurement of DNA Content within Cell Nuclei

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Liquid-Brush Cytology

Conventional Smear  Liquid-Based

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Liquid-Brush Cytology

- Better Representative Collection of Lesional Cells
- Easier Interpretation since Monolayer of Cells with the Elimination of Blood, and Obscuring Debris
- Decreased False-Positives and False-Negatives

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VITAL STAINING

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Vital iodine stain

• Vital iodine stain (3% lugol solution) has been used to determine the best site for biopsy in endoscopy of alimentary tract and cervix. It can also be used for oral cancer detection. This technique works on binding of iodine to glycogen granules in the cytoplasm, resulting in a black brown tissue color.
Toluidine blue (TB)

- Toluidine blue (TB) is a metachromatic dye that binds to nucleic acids (DNA or RNA) and can help to better visualization of high risk areas with rapid cell proliferation of oral SCC or OPL. This will guid the clinician to:
  - Detect carcinoma in situ and early invasive OSCC
  - Delination of surgical fields for biopsy sites
  - Detection of second primary cancers or satellite tumors
  - Recognition of post-treatment recurrence
**TBlue**

**Stained Lesion**

**Before:** Indistinct margin with lack of surface architecture

**After:** Lesion is easy to view, document and evaluate

Measure the stained lesion and document the staining pattern

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Light based detection system

Vizilit plus
Microlux DL

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1. CHEMILUMINESCENCE: Vizilite

2. TISSUE FLUORESCENCE IMAGING
   • LIGHT EMISSION TECH:
     I. MICROLUX DL
     II. ORASCOPTIC DK
     • NARROW EMISSION TISSUE FLORESCENCE (VELscope)
     • MULTIPLE FLUORESCENCE & REFLECTANCE (IDENTAFI 3000)
     • NEWER LIGHT BASED TECH
       I. CONTACT ENDOSCOPY
       II. ENDOSCOPIC HIGH FREQUENCY ULTRA SOUND

   • CELLULAR AND MOLECULAR TECH:
     I. CYTOMORPHOMETRIC & HISTOMORPHOMETRIC ANALYSIS
     II. MOLECULAR ANALYSIS
     III. GENETIC ALTERATION ASSESSMENT
Adjunctive Screening for Oral Soft Tissues

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How ViziLite Plus Works

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How it Works

Normal tissue produces fluorescence and appears as an apple-green glow

Abnormal epithelial tissue and underlying stromal disruption causes loss of fluorescence

Blue Excitation Light

Epithelium
Base ment Membrane
Stroma

Abnormal Epithelial Cells
Normal Epithelial Cells
Disruption of Stromal Collagen

Normal Stroma
Patient A

VELscope positive

Clinical Appearance

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Tissue fluorescence spectroscopy

- This technique consists of a small optical fiber that produces various excitation wave lengths and a spectrograph which receives and records on a computer and analyzes via a dedicated software, the spectra of reflected fluorescence from the tissue.
- This technique is very accurate in distinguishing normal mucosa from different lesions, but due to small size of optical fiber it is not practical to scan large areas of oral mucosa.
- Also it can not distinguish benign lesions from malignancy.

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Cellular and molecular techniques

- cytomorphometric and histomorphometric analysis
- molecular analysis
- genetic alteration assessment.

- These methods employ immunohistochemistry, histochemistry and immunologic techniques in detection of early changes. Yet these techniques are used for research purposes and are not clinically applicable.
BIOPSY (GOLD STANDARD)

1. Choose the best site for biopsy
2. Follow up a patient with a premalignant lesion
3. Screen for oral cancer in high risk patients or high risk sites of oral cavity (e.g. ventral tongue, floor of the mouth etc.)
4. Make a preliminary diagnosis when there is a systemic contraindication for surgical biopsy
5. Differentiation of pseudoepitheliomatosus hyperplasia from a real malignancy.

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ROLE OF ORAL PHYSICIAN IN MANAGEMENT OF ORAL CANCER
PALLIATIVE CARE IN ORAL CANCER

MOTHER TERESA

Even the rich are hungry for love, for being cared for, for being wanted, for having someone to call their own. - Mother Teresa

FAMILY, FRIENDS, RELATIVES

RADIO THERAPY

CHEMOTHERAPY

PHYSICIAN

RELIEF FROM PAIN AND OTHER SYMPTOMS

PATIENT

HYGIENE

NURSING CARE

COUNSELLING

COMMUNITY NURSING

SPIRITUAL

TOWARDS HAPPINESS

DIET

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Treatment

choice of treatment depends on such factors

• cell type and degree of differentiation
• Site
• Size
• location of the primary lesion;
• lymph node status;
• the presence of bone involvement;

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• the ability to achieve adequate surgical margins
• the ability to preserve speech
• the ability to preserve swallowing function
• the physical and mental status of the patient
• assessment of the potential complications of each therapy
• experience of the surgeon and radiotherapist
• personal preferences and cooperation of the patient
indications

- for tumors involving bone
- when the side effects of surgery are expected to be less significant than those associated with radiation
- for tumors that lack sensitivity to radiation
- for recurrent tumor in areas that have previously received a maximum dose of radiotherapy.
Radiation therapy

• Radiation therapy may be administered with intent to cure, as part of a combined radiation-surgery and/or chemotherapy management, or for palliation.
• total dose is high
• course of radiation is prolonged
• early and late radiation effects are common
Radiotherapy in palliative care

- radiation may provide symptomatic relief from pain, bleeding, ulceration, and oropharyngeal obstruction
• How radiation kills cell ??.....
Biologic effect of radiation

- dose per fraction
- number of fractions per day
- total treatment time
- total dose of radiation
- Methods for representing factors of dose
- fraction size
- time of radiation
- with a single calculation using the time-dose fraction (TDF)
- nominal standard dose (NSD) calculations have been described
Late complication due to....

- Effects on vascular, connective, and slowly proliferating parenchymal tissues.
- Late effects are related to the number of fractions,
- Fraction size
- Total dose
- Tissue type
- Volume of tissue irradiated.
- An increase in fraction size or a reduction in the number of fractions with the same total dose results in increased late complications, including tissue fibrosis and soft-tissue and bone necrosis.

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• more differentiated the tumor, the less rapid will be the response to radiotherapy.
• Exophytic and well-oxygenated tumors are more radiosensitive whereas large invasive tumors with small growth fractions are less responsive.
Advantage

• Treatment in situ
• avoiding the need for the removal of tissue
• may be the treatment of choice for T1 and T2 tumors
Types

- Brachytherapy
- External beam therapy /Teletherapy
- Conformal radiation therapy
• epithelial malignancies: radiation 1.8 to 2 Gy per fraction for 5 weeks to a total dose of 6,000 to 6,500 cGy.
• Hyperfractionation protocols vary, but 100 to 150 cGy often are delivered twice daily. Therapy can be accelerated to produce a total dose of 5,000 cGy in 3 weeks.
• Lymphomas in the head and neck usually are treated to a total dose of 3,500 to 5,000 cGy delivered at 180 to 200 cGy per day.
chemotherapy

- local therapies
- simultaneous chemoradiotherapy,
- adjuvant chemotherapy
- after local treatment
Objectives

- promote initial tumor reduction
- provide early treatment of micrometastases
Toxic effects

• mucositis
• nausea,
• vomiting
• bone marrow suppression.
Agents

- methotrexate
- bleomycin
- taxol and its derivatives
- cisplatin
- Platinum derivatives
- 5-fluorouracil

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Combined radiation and surgery

- advanced tumors
- tumors that show aggressive biologic behavior.
CAUSES OF PAIN IN ORAL CANCER

- Pain due to tumor
- Loss of epithelial barrier; ulceration; exposure of nerves
- Tumor necrosis; secondary infection
- Chemosensitization of nerves; pressure on nerves
- Tumor infiltration of bone, muscle, nerve, blood vessels
- Exacerbation of dental or periodontal disease

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• Pain due to cancer therapy
• Pain following surgery
• Acute surgical injury
• Secondary infection
• Myofascial or musculoskeletal syndromes
• Neuroma; deafferentation pain
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