Carcinoma of Tongue

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INTRODUCTION

• Oral carcinoma is fifth most common malignancy in head and neck globally.

• Oral cavity malignancies account for 20 per 100,000 population in India, out of which carcinoma tongue has a 4.6 in 100,000 and 1.8 in 100,000 incidence in males and females respectively.
Distribution of cancer in oral cavity

Occurrences

- Buccal mucosa: 32%
- Tongue: 22%
- Lower lip: 11%
- Palate: 11%
- Vestibule: 8%
- Alveolus: 5%
- Floor of mouth: 5%
- Upper lip: 3%
- Gingiva: 3%
• Carcinoma of the tongue has a higher risk of metastases to the regional lymph nodes and subclinical nodal metastases are found up to 30 % of T1 and T2.
ETIOPATHOGENISIS

• Tobacco abuse- dose dependent. (risk factor 4to5)
• Alcohol (risk factor 2) has synergistic effect (risk factor 15).
• In India tobacco chewing along with betel nut, lime contributes to 25% of cancers in oral cavity.
• Pooling of carcinogen contaminated saliva in the oral cavity is the main cause in these patients.
Etiology

• Tobacco contains a number of known carcinogens, e.g. polynuclear aromatic hydrocarbons and nitrosamines which cause DNA damage leading to gene mutations.
• Oral tobacco is mixed with betal leaf, slated lime and areca nut to form a quid called ‘paan’.
• The lime lowers the pH which accelerates the release of alkaloids from both the tobacco and areca nut.
• Alcohol causes DNA damage and gene mutation by a number of mechanisms. These include:

• Alcohol act as a solvent increasing the cellular permeability of tobacco carcinogens through the mucosa.

• The immediate metabolite of ethanol is acetaldehyde and this have a locally damaging effect on cells.

• Chronic alcohol use up regulates enzymes of the cytochrome P450 system which result in the activation of pro-carcinogens into carcinogens.
• Alcohol also decreases the activity of DNA repair enzymes resulting in increased chromosomal damage
• Alcohol impairs immunity due to a reduction in T cell number, decreased mitogenic activity and macrophage activity.
• Alcohol is high in calories, which suppresses appetite in heavy drinkers. Metabolism is further damaged by liver disease resulting in nutritional deficiencies and therefore lowered resistance to cancer.
OTHER CAUSES

- Poor oral & dental hygiene.
- Chronic irritation from sharp tooth, oral sepsis, spices
- Syphilis.
- Vit. A deficiency
- Marijuana - increasing incidence of tongue cancer seen in western world.
• HPV 16, 18, 31, 33, 35, 39 are associated with premalignant lesions and squamous cell Ca.
• HPV 16 and 18 are the most common types associated with squamous cell carcinoma.
• HPV bind to and inactivate tumour suppressor genes p53 and Rb.

➢ Fresh fruit, vegetables, antioxidants, vitamins A, C and E are protective
Site:

1. Lateral border of the anterior 2/3 of tongue - 25% each side.
2. Tip of tongue - 10%
3. Dorsum of tongue - 10%
4. Posterior 1/3 - 20%
5. Ventral surface of tongue - 5%
6. Tonsilolingual sulcus - 5%
Pathological relevance to surgeons

- Pathologically, Depth of infiltration is measured from the level of the *basement membrane* of the closest adjacent normal mucosa.
- A “*plumb line*” is dropped from this plane to the deepest point of tumor invasion.
Prognostic factors

- Primary tumor-depth of infiltration
  - perineural infiltration
- Nodes – volume
  - extranodal extension
Extranodal Extension (ENE)

• Pathological ENE is defined as extension of metastatic carcinoma from within a lymph node through the **fibrous capsule** and into the surrounding connective tissue, regardless of the presence of stromal reaction.

• Metastatic carcinoma that stretches the capsule but **does not** breach it does not constitute ENE
Premalignant lesions

• High Risk Lesions:
  – Erythroplakia
  – Chronic Hyperplastic Candidiasis

• Moderate Risk Lesions:
  – Oral submucous fibrosis
  – Syphilitic glossitis
  – Sideropenic dysphagia (Paterson – Kelly Syndrome)

• Low Risk:
  – Oral lichen planus
  – Discoid lupus erythematosus
  – Discoid keratosis congenita
Leukoplakia:

- Oral leukoplakia is defined by the WHO as “a white patch or plaque that cannot be scrapped off and also characterized clinically or pathologically as any other disease”.
Clinical forms of Leukoplakia

Homogenous

Non Homogenous
Malignant Transformation Potential

- Overall - 1 – 5%
- Homogenous - 0%
- Non Homogenous - 26%
Erythroplakia:

• Any lesion of the oral mucosa that presents as a bright red plaque which cannot be characterized clinically or pathologically

• Lesions are irregular in outline and separated from normal mucosa

• Incidence of malignant changes is 17 times higher than leucoplakia
• Chronic Hyperplastic candidiasis:
  - Produces dense plaques of leukoplakia
    – **High incidence of malignant transformation**
    – Believed to be invasion of Candida Albicans
Oral submucous fibrosis

• Progressive disease with fibrous bands beneath the mucosa $\rightarrow$ contracture $\rightarrow$ limited mouth opening $\rightarrow$ restricted tongue movement.

• Epithelium also shows dysplasia

• Mainly associated with areca nut usage than tobacco.
SPREAD

• **Direct**: to surrounding structures like floor of mouth, gums and mandible.
• **Lymphatic**: (rapid, early & very common)
• Perineural spread $\rightarrow$ leads to direct spread along cranial nerves.
• Angioinvasion $\rightarrow$ Distant metastasis.
CLINICAL FEATURES

• Painless long standing ulcer → Later becomes painful d/t infection or lingual nerve involvement
  – bleeds to touch
  – Induration present more than the ulcer area
  – Edge may be raised and everted.
• Excessive salivation: due to pain and inability to swallow
• Ankyloglossia: inability to protrude tongue with deviation to the affected side due to infiltration of muscles of the tongue, XI cranial nerve and / or floor of mouth.
• Dysphagia
• Dysarthria
• Halitosis
• Referred Otalgia
• Palpable Neck nodes
INVESTIGATIONS

• All lesions of the tongue and floor of mouth that last for longer than two to three weeks require biopsy to confirm the diagnosis.

• Similarly, all areas of leukoplakia and erythroplakia require a biopsy / excision (toludine blue).

• FNAC of suspicious/enlarged/palpable lymphnodes.
• **CECT scan** – for primary, cervical metastasis and infiltration of mandible.

• **MRI** – investigation of choice for imaging soft tissue infiltration and to detect perineural invasion.

• **X-ray chest** – for pulmonary metastasis.

• Routine investigation and immunological screening.
• Positron emission tomography (PET) is useful in improving the detection of distant metastasis in cases with large tumor volume and also for recurrent disease.
TNM Classification

- TX-Primary tumor cannot be assessed
- Tis-Carcinoma in situ
- T1-Tumor ≤2 cm, ≤5 mm depth of invasion (DOI) (DOI is depth of invasion and not tumor thickness)
- T2-Tumor ≤2 cm, DOI >5 mm and ≤10 mm or tumor >2 cm but ≤4 cm, and ≤10 mm DOI
- T3-Tumor >4 cm or any tumor >10 mm DOI
- T4- involvement of floor of mouth.

REGIONAL LYMPH NODES PATHOLOGIC CATEGORY CRITERIA

• Nx- Regional lymph nodes cannot be assessed

• N0- No regional lymph node metastasis

• N1- Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension and ENE-negative
• N2a- Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension and ENE-positive;
   Or More than 3 cm but not more than 6 cm in greatest dimension and ENE-negative;

• N2b-Metastases in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension and ENE-negative;

• N2c- Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, ENE-negative
• N3a- Metastasis in a lymph node more than 6 cm in greatest dimension and ENE-negative;
• N3b-Metastasis in a single ipsilateral lymph node more than 3 cm in greatest dimension and **ENE-positive**; (or) Metastasis in multiple ipsilateral, contralateral, or bilateral lymph nodes, with any **ENE-positive**
DISTANT METASTASIS

• Mx – can not be assessed
• M0 – no detectable distant metastasis
• M1 – distant metastasis present
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Types of TNM STAGING

- cTNM – clinical
- pTNM- pathological
- rTNM-(recurrent)
- RTNM-(residual)
Treatment- EARLY STAGE

• Stage 1 and 2- T1,N0,M0
  -T2,N0,M0

• SINGLE MODALITY TREATMENT:
  1) Surgery: Wide local excision (1.5 to 2cm unstretched normal mucosa all around the tumour) and Selective Neck Dissection (level I to III) OR
2) Teleradiotherapy + Brachytherapy
• total of 6000 to 7000 rads in a period of 6 to 7 weeks.
TREATMENT - Advanced Stage

• Stage III - T1,2,3 N1 M0
  T3 N0 M0
• Stage IV – T1,2,3 N2,3 M0
  T4 N0 M0

COMBINED MODALITY TREATMENT:
Surgery + Postoperative Chemoradiation

1) Wide local excision with Reconstruction + Radical neck dissection followed by post operative Chemoradiation.
• Reconstruction:
  • Pectoralis Major Myocutaneous FLAP-PEDICAL flap
    - Forearm free flap
    - Fibular free flap, if mandible is also excised.
• Chemoradiation:
  • radiation 5000 to 6000 rads for 5 days/week.
  • On 6th day – chemotherapy
Management of neck nodes:

• Clinically node negative:
  – Cervical nodes may have occult metastasis up to 30% even if clinically node negative
  – Hence Selective Neck dissection “Supraomohyoid dissection” (levels 1, 2, 3) as a sampling procedure to be done.
  – If nodes are positive – completion neck dissection or radiation therapy given.

• Clinically node positive:- radical neck dissection.
SURGERY

• Advantages:
  – Short period treatment
  – Control of margins
  – Specimen available for HPE/DOI
  – Helps in planning adjuvant treatment
  – No radiation sequelae

• Disadvantages:
  – Tissue and functional loss
  – Disfigurement
  – Bleeding & infection
Rehabilitation

• Swallowing Therapy
• Speech Therapy
• Jaw stretching exercise after radiotherapy.
Radiotherapy

RT & surgery have equal success in early lesion. RT can be given:

- Brachytherapy
- Tele therapy – EBRT
- Combination therapy
- RT help in organ preservation but long term complication are significant
• Post operative RT is preferred over pre operative because of effect on wound healing
• Per operative RT: inoperable, unfit for surgery & down staging
• Post RT is indicated in patients with
  – T3/T4 primary
  – positive surgical margins
  – perineural, perilymphatic vascular invasion
  – microscopic gross residual tumor
  – extra capsular spread
• Disadvantage – no specimen for HPE
• Altered taste, xerostomia and the protracted nature of treatment course.
• Requires at least 6 weeks of treatment.
• Osteonecrosis of mandible.
• Newer technique of IMRT and brachytherapy reduces above side effects.
• ADVANTAGE- Provide better functional result with speech.
CHEMOTHERAPY

- As a adjuvent to RT

  • Palliative
    – Recurrence
    – Metastatic disease

  • Drugs: Cisplatin, MTX, 5FU
Follow up

• Every 2 months- for 6 months
• 3 monthly- upto 2 years
• 6 monthly-upto 5 years
• Yearly – after 5 years

Look for-
-Recurrence ,
-2\textsuperscript{nd} primary
-Hypothyroidism due to postop radiotherapy
-Rehabilitation
Predictors of Poor prognosis:

**Past**
- Increasing tumor thickness (>4mm)
- Poorly differentiated
- High grade tumors
- Perineural, Vascular and lymphatic invasion
- DNA ploidy status such as aneuploid carry worst prognosis
- Verrucuous Ca has better prognosis

**Latest**
- Depth of infiltration
- Perineural, Vascular and lymphatic invasion
- Human papilloma virus
PROGNOSIS

• Stage 1: 80 – 90 %
• Stage 2: 70 – 80 %
• Stage 3: 30 – 50 %
• Stage 4: 20 – 30 %
PREVENTION

• Primary prevention is better.
• Secondary prevention:
  - Cancer screening regularly for early detection
  - Regular follow up to decrease morbidity.
THANK YOU
Examination

• General EXAMINATION :
• Examination of oral cavity:

• Site , size, margins,
• Colour , texture,

• mobility of tongue
• **Homogenous:**

Uniform flat appearance that may exhibit shallow cracks and has a smooth, plaque like, wrinkled or corugated surface with a consistent texture throughout.
Non Homogenous (speckled)

- A predominantly white or white and red lesion (erythroleukoplakia).
- Area of redness and ulceration
- Irregularly flat, nodular thickening and exophytic
- Nodular lesions have raised, rounded red and or white excrescences