Cancer of the lip, tongue and floor of mouth

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Part 1. The Lip

**Introduction**

- Squamous cell carcinoma forms the predominant histological variant, followed by melanoma and carcinoma of minor salivary gland.

- Keratinocyte is the cell of origin, with DNA mutation arising spontaneously or through a variety of mutagens (chemical, physical or microbial).

- Lip cancer constitutes 30% of malignant tumors of the oral cavity, in sunbelt areas it is only second to skin cancer of head and neck in incidence.

- 95% occur in male (older), 89% occur in the lower lip (sun exposed), 7% in the upper lip and 4% in the commissures.
Fig. 5.1 Site and gender distribution: squamous cell carcinoma of the lips.

Fig. 5.2 Histologic distribution: carcinoma of the lips.
Risk factors:

- Tobacco\(^1\)\(^2\) - 25%
- Alcohol - 7-19%
- Betel quid - 20%
- Micronutrient def. - 10-15%
- Remainder:
  - by radiation exposure
  - infections (HPV\(^3\), syphilis, candidosis)
  - Poor oral hygiene
  - Immunocompromised
  - Genetics: Fanconi anaemia, dyskeratosis congenital,
Anatomy:

Surface:

- Cupid's Bow
- Philtrum
- Vermillion Border
- Oral Commissures
Anatomy:

Saggital section:
Discussion:

• Contralateral neck metastasis from upper lip cancer is exceedingly rare (as two lateral separated segments form).

• Versus the lower lip where it's formed by the fusion of two lateral mandibular processes in the midline.

• Blood supply is provided by the superior and inferior labial arteries and branches of the facial a.
• The labial a. form an arcade around the oral cavity such that lesions in the **lateral aspect** of the lip receive blood supply from both the medial and lateral regions.

• **Sensory supply** to the skin (maxillary) and vermillion border (mandibular) of trigeminal n.

• **Muscular control** of the orbicularis oris and levators and depressors of the oral commissure by the facial n.
Lymphatic drainage:

- **lesions of lateral aspect of the upper lip:**
  1. Buccal and periparotid lymph nodes
  2. Prevascular facial nodes (overlying the body of mandible)
  3. Level 1 (submandibular triangle)
  4. Deep Jugular chain

- **lesions of the lower lip:**
  1. Level 1 nodes (submental and submandibular)
  2. Prevascular facial nodes
  3. Deep Jugular nodes at level 2 and 3, rarely to level 4, 5
Lymphatics of the neck:

- Internal Jugular V.
- Sternocleidomastoid m.
Clinical characteristics

- Any solitary oral lump, ulcer, white or red lesion persisting for more than 3 weeks (4), or non-healing socket. Numbness, or unexplained loose tooth should be regarded as cancer until proven otherwise (5).

- A characteristic ulcerated or exophytic cauliflower-like lesion on the vermilion border, with varying degrees of infiltration of contiguous structures (e.g., skin, labial mucosa, mandible).

- The primary lesions may be; ulcerative, exophytic or endophytic.
Clinical summary:

- red lesion (erythroplasia or erythroplakia)
- mixed red/white lesion (erythroleukoplakia); irregular white lesion (verrucous leukoplakia)
- lump
- ulcer with fissuring or raised exophytic margins
- pain or numbness
- abnormal blood vessels supplying a lump
- loose tooth
- extraction socket not healing
Diagnosis:

- **Diagnostic aids:**

<table>
<thead>
<tr>
<th>Established utility</th>
<th>Potential utility</th>
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<tbody>
<tr>
<td>Biopsy and histopathological</td>
<td>Vital staining</td>
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<tr>
<td>examination</td>
<td>Optical techniques (e.g. Vizilite; Velscope)</td>
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<td>Brush biopsy</td>
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<td>DNA ploidy (chromosomal polysomy)</td>
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<td>Molecular markers</td>
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<td>Salivary biomarkers</td>
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- Unfortunately none of the visual diagnostic aids have yet proved **superior** to a good oral examination with conventional histopathology(6).
Exophytic lesion:
growing outward, proliferating externally or on the surface epithelium of an organ or other structure in which the growth originated.

Ulcerative lesion
Ulcerative lesion:
Cauliflower-like lesion:
Special investigations:

Radiography:

- In early stage tumors radiographic evaluation is not indicated.

- Advanced tumors that adhere to or invade the mandible require investigations such as panoramic x-ray, or for more detailed evaluation CT scan or Dentascan (extent of bone invasion).
Staging

Primary tumor (T)
TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Tis Carcinoma in situ

T1  Tumor ≤2cm in greatest dimension
T2  Tumor >2cm but ≤4cm in greatest dimension
T3  Tumor >4cm in greatest dimension
T4a Moderately advanced, local disease
Lip - Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face

T4b Very advanced, local disease
Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

Nodal staging is according to group involved as described before.

- Only 10% of patients present with clinically palpable cervical lymph node metastasis.
Stage distribution:

Fig. 5.7 Stage distribution: squamous cell carcinoma of the lips.
4. Treatment:

- Treatment goals:
  - Long-term control of cancer with preservation of competency of the oral cavity and esthetic appearance.
- Multi-discipline team that requires co-ordinated and methodical planning.

- Factors affecting choice of treatment:
  1. Size (T-stage) of primary tumor
  2. Extent of lip resection necessary
  3. Method of reconstruction
factors continued:

1. Anticipated esthetic and functional result of reconstructive surgery
2. General medical condition of patient
3. Long-term impact of surgery or radiotherapy as initial treatment
4. cost and convenience of treatment and compliance of the patient
5. Histology- as squamous carcinomas and BCC can be irradiated, where by melanoma, minor salivary gland carcinomas and malignant tumors of soft somatic tissues can't be.
Treatment options (lower lip):

1. 'V'- excision of the lower lip
2. Lip Shave - Areas of leukoplakia with keratosis and superficially invasive or in situ carcinomas
3. Abbe-Estlander flap repair
4. Karapandzic Flap repair
5. Bernard reconstruction
6. Radical resection and microvascular free flap

Upper lip repair:

1. Nasolabial flap repair
2. Resection and reconstruction with unilateral burrows triangle repair.
3. Bilateral Burrows triangle repair
Procedures:

‘V’ – Excision of the lower lip:
For small superficial (T1/T2) lesions involving the vermilion border and the underlying musculature:
• **A note on closure of the lip: (3 layer closure):**
  – 1\textsuperscript{st} Mucosal
  – 2\textsuperscript{nd} muscular
  – 3\textsuperscript{rd} skin with particular attention to maintain the integrity of the Gray line.
• **Abbe-Estlander flap repair:**
  – When more than 30% of the width of the lip is resected, reconstruction of the lip requires mobilization of a flap from the opposite lip:

*Fig. 5.39 The proposed lines of incision for resection of the tumor and elevation of the flap.*
Fig. 5.43 A fine nylon suture is taken through the vermilion edges for accurate alignment.
Fig. 5.45 Closure of the skin incisions.
Results of treatment

• Since a majority of patients present at an early stage for diagnosis and treatment, excellent results are achieved by appropriate initial therapy.

• Approximately 15% of patients fail initial therapy with local recurrence and regional lymph node metastasis being the most common sites of failure.

• Salvage treatment is often successful and should be aggressively undertaken for this tumor.
Pattern of failure:

Fig. 5.98 Patterns of failure: squamous cell carcinoma of lips.
Part 2. Tongue:

• Introduction:

  – The tongue and Floor of the mouth are the most common sites of origin for primary squamous cell carcinomas in the oral cavity in the western world. The predominant tumour of the tongue is squamous cell carcinoma, most of which are well differentiated.

  – Typically a disease of middle-aged or elderly patients and usually presents as a painless lesion.

  – Tobacco and alcohol(to a greater extent) are important aetiological factors.

  – Approximately 50% arise from the anterior two-thirds of the tongue of which 85% occur on the lateral border.
Site distribution of OSCC:

Fig. 6.6 The site distribution of primary cancers in the oral cavity and the oropharynx.
Extrinsic and intrinsic muscles of the tongue:

Extrinsic muscles:
Intrinsic muscles:
Floor of mouth:
Premalignant lesions:

1. Leukoplakia

2. Erythroplakia

3. Lichen planus

“Potentially malignant” was the term preferred above “premalignant or precancerous” as defined in a WHO workshop held in 2005.
1. Leukoplakia

- “A white patch or plaque that cannot be characterised clinically or pathologically as any other disease” (WHO), it’s strictly a clinical diagnosis. (doesn’t imply specific histopathological alterations.)

- Leukoplakia is six times more common among smokers than non-smokers.
Clinically, leukoplakia can be subdivided into a:

1. **homogeneous type (1% malignant transformation)**
   - (flat, thin, uniform white in colour)

2. **non-homogenous type: (> 1% malignant transformation)**
   - a white-and-red lesion (*erythroleukoplakia*), that may be either irregularly flat (speckled) or nodular.
   - **Verrucous leukoplakia**: although homogenous in appearance, it displays a verrucous texture.
Histopathologically a distinction between dysplastic and non-dysplastic leukoplakia can be made. There are 5 stages in epithelial precursor lesions.
Treatment of leukoplakia:

Table 7
Management of leukoplakia

LEUKOPLAKIA
(Provisional clinical diagnosis C1*)

- Elimination of possible cause(s), including tobacco habits (2-4 weeks to observe the result)
- No possible cause(s) (Definitive clinical diagnosis: C2)

Good response

- No response (Definitive clinical diagnosis C2)

- Biopsy

Histopathologically proven diagnosis
(By exclusion of "other known lesions"; C3 or C4)

- Known lesion
  - Management accordingly

- Non-dysplastic leukoplakia
  - Treatment (if feasible, e.g. < 2-3 cm)
    - Follow-up in both treated and untreated patients at intervals of 6 months; lifelong (?)

- Dysplastic leukoplakia
  - Treatment (if feasible, e.g. < 2-3 cm)
    - Follow-up in both treated and untreated patients at intervals of 3 months; lifelong (?)

* C = certainty factor
2. Erythroplakia:

- **Defined:** “fiery red patch that cannot be characterized clinically or pathologically as any other definable disease.

- **Clinically:** appears as a flat or depressed lesion with a smooth or granular surface. It occurs mainly in the middle aged and elderly, usually as a solitary lesion anywhere in the oral cavity.

- **Histopathologically,** shows some degree of dysplasia and frequently even carcinoma in situ or invasive carcinoma. The majority will undergo malignant transformation.

- **Treatment:** Laser or cold knife with no guidelines with regard to the width of the surgical margins.
Erythroplakia
3. **Lichen Planus:**

An eruption of shiny flat-topped purplish (usually itchy) papules on the wrist and forearms and thighs

- There is an ongoing debate as to whether OLP carries a malignant risk.
Summary of potential malignant disorders:

<table>
<thead>
<tr>
<th>Approximate malignant potential</th>
<th>Disorder</th>
<th>Known aetiological factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high (85%+)</td>
<td>Erythroplakia</td>
<td>Tobacco/alcohol</td>
</tr>
<tr>
<td>High in some instances (30%+)</td>
<td>Actinic cheilitis</td>
<td>Sunlight</td>
</tr>
<tr>
<td></td>
<td>Chronic candidosis (candidal leukoplakia)</td>
<td><em>Candida albicans</em></td>
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<td></td>
<td>Dyskeratosis congenita</td>
<td>Genetic</td>
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<tr>
<td></td>
<td>Leukoplakia (non-homogeneous)</td>
<td>Tobacco/alcohol</td>
</tr>
<tr>
<td></td>
<td>Proliferative verrucous leukoplakia</td>
<td>Human papillomavirus (HPV)?: most often no history of tobacco/alcohol</td>
</tr>
<tr>
<td></td>
<td>Sublingual keratosis</td>
<td>Tobacco/alcohol</td>
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<tr>
<td></td>
<td>Submucous fibrosis</td>
<td>Areca nut</td>
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<tr>
<td></td>
<td>Syphilitic leukoplakia</td>
<td><em>Treponema pallidum</em></td>
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<tr>
<td></td>
<td>Xeroderma pigmentosum</td>
<td>Genetic</td>
</tr>
<tr>
<td>Low (&lt;5%)</td>
<td>Atypia in immunocompromised patients</td>
<td>HPV</td>
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<tr>
<td></td>
<td>Diabetes</td>
<td>Idiopathic</td>
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<td></td>
<td>Discoid lupus erythematosus</td>
<td>Autoimmune</td>
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<tr>
<td></td>
<td>Fanconi syndrome</td>
<td>Genetic: anaemia</td>
</tr>
<tr>
<td></td>
<td>Leukoplakia (homogeneous)</td>
<td>Friction/tobacco/alcohol</td>
</tr>
<tr>
<td></td>
<td>Lichen planus</td>
<td>Idiopathic</td>
</tr>
<tr>
<td></td>
<td>Paterson–Kelly-Brown syndrome (sideropenic</td>
<td>Iron deficiency</td>
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<tr>
<td></td>
<td>dysphagia: Plummer–Vinson syndrome)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Scleroderma</td>
<td>Autoimmune</td>
</tr>
</tbody>
</table>
Clinical characteristics and diagnosis:

- Macroscopically the lesions appear as either exophytic or endophytic or superficial proliferative (ulcerative).

- **Bleeding** form the surface of the lesion is a characteristic for malignancy.
Treatment:

• As with lip cancer a multi-disciplinary approach is very essential for optimal results.

• Factors affecting choice of treatment:

  1. Tumor factors
  2. Patient factors
  3. Physician factors
1. Tumor factors:

- Primary site
- Size (T Stage)
- Location (anterior versus posterior)
- Proximity to bone (marginal mandibulectomy and mandibulotomy)
- Status of cervical lymph nodes
- Previous treatment
- Histology (type, grade and depth of invasion)
Primary Site:

- Cancers of the oral tongue, floor of the mouth are at high risk of regional lymph node metastases v. lip.

Size:

- Small superficial primary tumors are easily accessible for surgical resection

- With increasing size, the risk of regional lymph node metastases increases even with the clinically negative neck (micrometastases)
Location:
• Lesions located in the anterior part of the oral cavity have a lesser risk of dissemination to regional lymph nodes.

• **Cervical lymph Nodes:**
  - Extend of nodal metastases and location of palpable lymph nodes determines extend of neck dissection

  - The 1st echelon lymph nodes are at levels 1, 2, and 3 with infrequent dissemination to level 4 (skip metastases to level 5 does not occur).

  - Thus elective clearance for micrometastases does not involve level 5

  - Gross metastases in the anterior triangle requires a comprehensive dissection of all 5 levels.
• **Previous treatment:**
  – Radiation therapy previously delivered to the same area for a different lesion may not be available to treat a second tumor in the same area

• **Histology:**
  - All other primary malignant tumors in the oral cavity except for lymphoma are treated by surgery.

- **Depth:** heavily impacts treatment and prognosis
  In situ and **superficially invasive** – lower risk regional node involvement and highly curable.
  **Thicker lesions** have increased risk with adverse impact on prognosis(7)
Risk of nodal metastases and death in relation to thickness of primary squamous cell carcinoma

Figure 2. Risk of nodal metastases and death in relation to thickness of primary squamous cell carcinomas of the tongue and floor of mouth (adapted from Spiro et al.⁵).
Selection of initial treatment:

– Stage T1 and T2: single modality treatment (surgical resection or radiotherapy)

– Stage 3/4: Surgical resection with immediate appropriate reconstruction and postoperative radiotherapy.

– Radiotherapy after surgical resection, offers better or comparable local and regional control rates of cancer over preoperative radiotherapy.
Surgical approaches to the oral cavity:

– Peroral laser excision of leukoplakia, if lesions are focal and limited in surface extent.

– Partial glossectomy: all T1 and T2 lesions of the anterior 2/3 of tongue

– T3/T4 if boney involvement mandibulectomy, with regional lymph node neck dissection. Depending on TNM staging

– Extracapsular extension of disease in metastatic cervical lymph nodes and those who have positive margins benefit greatly from chemotherapy and radiotherapy Versus radiotherapy alone(8).
2. Patient factors:
   • General medical condition
   • Tolerance of treatment
   • Occupation of patient
   • Acceptance and compliance
   • Lifestyle (smoking and drinking)
   • Older age is not a contra-indicator but needs to be considered with associated co-morbidities
Physician factors:

Figure 7. Role of various specialists during the life of a patient with head and neck cancer.
Outcomes of surgical treatment of oral cancer
• Most important factor which affects long term outcome following initial treatment of oral cancer is the stage of disease at the time of presentation.
Sentinel lymph node biopsy:

• SLNB is a minimally invasive technique, performed in conjunction with radiotracer injection and lymphoscintigraphy.
• Allows identification and excision of targeted upper echelon lymph nodes that drain the site of a primary malignancy of otherwise subclinical nodal metastases.
• SLNB offers the potential for more anatomically accurate surgery based on each patient’s unique lymphatic drainage pattern
• It has been demonstrated to have an excellent safety profile with good sensitivity in identifying occult neck metastases
• Thank you
References:

References continued:

• 10. Isaäc van der Waal *Potentially malignant disorders of the oral and oropharyngeal mucosa; Oral Oncology 45 (2009) 317–323.
• 12. Jatin Shah, head and neck surgery and oncology 3rd edition