Case: History

- **HPI:** 81F presents with left facial swelling, difficulty chewing, dentures no longer fitting, & weight loss x 3 months. 30 PY smoking hx.
- **PE:**
  - **ECOG:** 2, dementia but independent in ADLs
  - **HEENT:** Edentulous, white left intraoral mass, exophytic and firm arising from left buccal mucosa.
  - **Lymphatic:** No cervical, submandibular, submental, or supraclavicular lymphadenopathy
Common Presentations:

- Oral cavity pain
- Facial swelling
- Dysgeusia, tongue immobility/deviation
- Dysphagia
- Trismus
- Speech changes
- Loose teeth
- Poorly fitting dentures
- Hx of alcohol, tobacco, betel nut use
- Cranial nerve deficits:
  - CN V2-V3 – Trismus, impaired sensation of middle and/or lower third of face, paresthesias, impaired muscles of mastication
Case: Imaging + Biopsy

- CT neck w/ contrast: 4.6 x 3.2 x 3.9 cm left inner cheek heterogeneously enhancing mass eroding into the left mandible
- CT chest: No metastatic disease
- ENT performed incisional biopsy: well-differentiated, keratinizing invasive SCC
Workup & Evaluation

- H&P: complete H&N exam, FOL as clinically indicated (e.g., BOT involvement), tobacco/EtOH use
- CT neck with contrast and/or MRI
- CT chest; consider PET systemic staging
- Core or incisional bx of primary tumor vs FNA of palpable nodes; consider exam under anesthesia
- Dental, speech therapy, nutrition evaluations
- Multidisciplinary consultation: ENT, oral surgery, radiation oncology, medical oncology, nutrition
- Tobacco cessation counseling
- Psychosocial evaluation
- HPV etiology rare and not typically tested
Oral Cavity Cancer: Epidemiology

- Deaths: 10,030 in US
- 80% due to tobacco and EtOH
  - Tobacco: 3x higher risk
  - EtOH + tobacco: 10-15x higher risk
- Most commonly oral tongue in US (40-50%)
- Buccal cancer common in Asia due to betel/tobacco chewing
- Median age at diagnosis: 62
  - Most cases at age > 50
- Median age at death: 68
• Oral cavity = Cavity bounded by alveolar margins of maxilla and mandible
• Roof: hard palate anteriorly and soft palate posteriorly
• Floor: mylohyoid muscle; anterior 2/3 of tongue on floor
Anatomy: Oral Cavity

- See also for radiographic anatomy:
## Oral Cavity Cancer: T Staging

<table>
<thead>
<tr>
<th>T stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T0</strong></td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td><strong>T1</strong></td>
<td>(&lt; 2) cm size (\text{AND}^*) (\leq 5) mm depth</td>
</tr>
<tr>
<td><strong>T2</strong></td>
<td>(&lt; 2) cm size (\text{AND}) depth (\geq 5) mm but (\leq 10) mm (\text{OR}) (&gt; 2) cm but (&lt; 4) cm with depth (\leq 10) mm</td>
</tr>
<tr>
<td><strong>T3</strong></td>
<td>Tumor (&gt; 4) cm (\text{OR}) (&gt; 10) mm depth</td>
</tr>
<tr>
<td><strong>T4</strong></td>
<td>Locally advanced disease</td>
</tr>
<tr>
<td><strong>T4a</strong></td>
<td>Moderately advanced local disease (e.g. invades through cortical bone, inferior alveolar nerve, FOM/intrinsic tongue muscles, skin of face, maxillary sinus)</td>
</tr>
<tr>
<td><strong>T4b</strong></td>
<td>Very advanced local disease (e.g. invades masticator space, pterygoid plates/spaces, skull base, encases internal carotid artery)</td>
</tr>
</tbody>
</table>

*AJCC 8th edition includes depth of invasion (DOI)*
Oral Cavity Cancer: T Staging

• Depth of invasion (DOI) versus Tumor Thickness
  – DOI = perpendicular distance from the basement membrane region to the deepest point of the infiltrative front of the tumor
  – Tumor Thickness = perpendicular distance between the highest point of the tumor surface to the deepest point of the infiltrative front of the tumor
Oral Cavity Cancer: N Staging

<table>
<thead>
<tr>
<th>N stage, AJCC 8th edition</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N0</strong></td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td><strong>N1</strong></td>
<td>Metastasis in a single ipsilateral lymph node, ≤ 3 cm, ENE-</td>
</tr>
<tr>
<td><strong>N2</strong></td>
<td>Single ipsilateral LN (&gt; 3 cm but ≤ 6 cm) or multiple LN (≤ 6 cm)</td>
</tr>
<tr>
<td><strong>N2a</strong></td>
<td>Metastasis in single ipsilateral lymph node (&gt; 3 cm but ≤ 6 cm)</td>
</tr>
<tr>
<td><strong>N2b</strong></td>
<td>Metastasis in multiple ipsilateral lymph nodes (all ≤ 6 cm)</td>
</tr>
<tr>
<td><strong>N2c</strong></td>
<td>Metastasis in bilateral or contralateral lymph nodes (all ≤ 6 cm)</td>
</tr>
<tr>
<td><strong>N3</strong></td>
<td>Metastasis in a lymph node &gt; 6 cm and ENE- <strong>OR</strong> clinically overt ENE+</td>
</tr>
<tr>
<td><strong>N3a</strong></td>
<td>Metastasis in a lymph node &gt; 6 cm and ENE-</td>
</tr>
<tr>
<td><strong>N3b</strong></td>
<td>Clinically overt ENE+</td>
</tr>
</tbody>
</table>

*N3 in AJCC 8th edition is now N3a and N3b*
Oral Cavity Cancer: Stage Grouping

<table>
<thead>
<tr>
<th>AJCC 8th Edition Stage Grouping</th>
<th>0</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IVA</th>
<th>IVB</th>
<th>IVC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tis</td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td>T4a</td>
<td>Any T</td>
<td>Any T</td>
</tr>
<tr>
<td></td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0 or N1</td>
<td>N0, N1, or N2</td>
<td>N3</td>
<td>Any N</td>
</tr>
<tr>
<td></td>
<td>M0</td>
<td>M0</td>
<td>M0</td>
<td>M0</td>
<td>M0</td>
<td>M0</td>
<td>M1a or M1b</td>
</tr>
</tbody>
</table>
Case: Management

• Early stage lesions (T1-2, N0-1)
  – Surgery preferred
  – Definitive (chemo)radiation therapy for inoperable patients

• Locally advanced lesions (T3-4, N+)
  – Surgical resection +/- radiation
    • Add concurrent chemotherapy for ECE or + Margins
  – Definitive chemoradiation if unresectable
Case: Surgical Management

- Stage IVA disease (cT4aN0M0) based on mandibular cortical bone invasion
- Surgery:
  - Radical resection of left buccal mucosa, FOM, and segmental mandibulectomy with sLND (IA, left IB-III, 0/22 LN) with indeterminate margins, 14 mm depth of invasion
- Neck dissection routinely includes 1st echelon nodes in level I-III; levels IV-V may be dissected if nodal disease discovered in surgery
- Ipsilateral dissection for well cN+ lateralized primary sites; for midline primary or invasion of a midline OAR consider bilateral neck dissection
- Neck dissection when cN+
  - Consider for N0 patients if DOI > 3mm
Oral Cavity Cancer: Surgical Management

• Should patients with oral cavity cancer have up front neck dissection?

• D’Cruz et al, NEJM 2015:
  • n=496 patients with T1-T2, cN0 SCC
  • Randomized:
    • Oral excision (> 5 mm margin) w/ modified neck dissection (levels 1 – 4) if nodal relapse
    • Oral excision + ipsilateral selective neck dissection (levels 1 – 3) + included levels 4 – 5 if LN+ during surgery
    • PORT as clinically indicated

Improved OS with planned neck dissection
Case: Post-Operative Management

• What is the role of adjuvant chemoradiation vs RT alone for this patient?

  – Bernier, Cooper et al. *Head and Neck* 2005:

    Pooled analysis of EORTC 22931 and RTOG 9501: OS improved with RT + concurrent chemo (RCT) vs RT alone for patients with +Margin and/or +ENE

<table>
<thead>
<tr>
<th># at Risk</th>
<th>Year</th>
<th>0</th>
<th>2</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT</td>
<td></td>
<td>122</td>
<td>82</td>
<td>31</td>
</tr>
<tr>
<td>RT</td>
<td>---</td>
<td>111</td>
<td>59</td>
<td>16</td>
</tr>
</tbody>
</table>
Case: Post-Operative Management

• What is the role of chemoradiation vs RT alone for this patient?
  – MACH-NC Meta-Analysis (Pignon et al, Radiother Oncol 2009):

  Significant OS benefit with addition of chemotherapy per MACH-NC. **Absolute difference at 5 years = 5.1%**
Case: Post-Operative Management

• What is the role of chemoradiation vs RT alone for this patient?
  – HOWEVER:
    • Poor performance status (ECOG 2)
    • Advanced age (81)
    • Comorbid dementia
• Therefore, **post-operative RT alone** was utilized despite indeterminate margin
• Typical **PORT Indications:**
  – + Margins / Gross residual disease
  – T3/T4
  – LVSI
  – PNI
  – >1-3 LNs
  – DOI > 3mm
Radiation Technique

• Post-operative RT with a composite IMRT/VMAT plan

• Prescription:
  – 50 Gy in 2.5 Gy/fraction to the high risk CTV (tumor bed with margin)
  – 40 Gy in 2.5 Gy/fraction to low risk CTV (tumor bed with additional margin) + undissected right level IB

• Conventional fractionation (most commonly utilized) dose prescription = 60-66 Gy to high/intermediate risk CTVs and 54 Gy to low risk CTV at 2 Gy/fraction

• Alternative techniques include protons & brachytherapy
Radiation Simulation

• Position: Supine in short thermoplastic mask, bite block
  – If treating neck, utilize long thermoplastic mask
• CT with IV contrast
• Consider wiring scars, bolus, based on high risk features
• Fuse pre-op CT/MRI to delineate initial tumor bed for CTV design
Radiation Technique: Hypofractionation

- **Goal**: Deliver accelerated treatment without chemotherapy to provide maximal local control benefit with minimized acute toxicity → hypofractionation
- Common at our institution for smaller PTV volume and pN0 disease
- 46 – 50 Gy at 2 Gy/fx + boost at **2.5 Gy/fx without chemotherapy**
  - Total 55 Gy (neg. margin)
  - Total 62.5 Gy (pos. margin)
- 3 year LRC =
  - 87% intermediate risk
  - 66% high risk
- Hypofractionation experiences with concurrent chemotherapy:

<table>
<thead>
<tr>
<th>Intermediate risk</th>
<th>ECE or Microscopic + margin + 1 risk factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>ECE and Microscopic + margin; or ECE or +margin and ≥ 2 risk factors</td>
</tr>
</tbody>
</table>
Radiation Technique: Elective Nodal Coverage

• Pathologic nodal disease by T Stage and site for cN0 neck

<table>
<thead>
<tr>
<th>Site</th>
<th>Tx-T1-T2</th>
<th>T3-T4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral tongue (n=48)</td>
<td>18.6%</td>
<td>31.6%</td>
<td>25%</td>
</tr>
<tr>
<td>FOM (n=62)</td>
<td>18.6%</td>
<td>26.3%</td>
<td>21%</td>
</tr>
<tr>
<td>Lower gum (n=41)</td>
<td>11.5%</td>
<td>13.3%</td>
<td>12.2%</td>
</tr>
<tr>
<td>Buccal mucosa (n=10)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Retromolar trigone (n=23)</td>
<td>36.4%</td>
<td>33%</td>
<td>34.8%</td>
</tr>
</tbody>
</table>

• Should the undissected level IV be included in RT fields?
  – Warshavsky et al, JAMA OHNS 2019
  – Rate of level IV involvement in cN0 neck is 2.53% in fixed-effects model
    → therefore omitted in this patient
Radiation Contouring

• GTV-Preop = initial site of gross disease as estimated by preoperative imaging
• CTV50 (high risk) = Pre-op GTV / tumor bed with margin (5-10 mm)
• CTV40 (low risk) = CTV50 + 5-10 mm expansion based on clinical suspicion and uncertainty due to post-op anatomical changes and encompassing surgical clips + undissected right IB
• PTV = CTV + 3mm margin, based on daily image guidance and immobilization
• For contouring/dose guidelines with conventional fractionation/SIB see: https://econtour.org/cases/28
Case: Target Volumes

GTV – Pre-op
CTV40 – Low risk
CTV 50 High risk
Case: Target Volumes

GTV – Pre-op
CTV40 – Low risk
CTV 50 High risk
Case: Target Volumes

- GTV – Pre-op
- CTV40 – Low risk
- CTV 50 High risk
Case: Target Volumes

GTV – Pre-op
CTV40 – Low risk
CTV 50 High risk
Key Dose Constraints: Hypofractionation

<table>
<thead>
<tr>
<th>OARs</th>
<th>Dose</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rt Parotid</td>
<td>5-8 Gy</td>
<td>Median Preserve major salivary gland</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>30-35 Gy</td>
<td>Median Mucositis, pain</td>
</tr>
<tr>
<td>Larynx</td>
<td>15 Gy</td>
<td>Median Wound healing around tracheostomy, hoarseness</td>
</tr>
<tr>
<td>Pharynx</td>
<td>25-30 Gy</td>
<td>Median Mucositis, pain</td>
</tr>
<tr>
<td>Mandible</td>
<td>56 Gy</td>
<td>Max Osteoradionecrosis</td>
</tr>
<tr>
<td>Cochlea, left</td>
<td>30 Gy</td>
<td>Max Ototoxicity</td>
</tr>
<tr>
<td>Left eye</td>
<td>30 Gy</td>
<td>Max Vision loss</td>
</tr>
<tr>
<td>Pharyngeal constrictors</td>
<td>25-30Gy</td>
<td>Median Post-op swallowing</td>
</tr>
<tr>
<td>Rt SMG</td>
<td>No constraint</td>
<td>In PTV 40 target volume</td>
</tr>
</tbody>
</table>
Case: On Treatment Management

**Surgical**
- **Tracheostomy**
  - Airway protection post-op
- **Dobhoff/NGT or PEG**
  - Allow intra-oral healing post-op and with RT induced mucositis
  - Speech & swallow evaluation for aspiration risk
- **Wound healing**
  - Ensure flap is well healed prior to RT to minimize wound complication and RT breaks

**Radiation / Chemoradiation**
- **Pain management**
  - Secondary to post-op pain and RT-induced mucositis
- **Xerostomia**
  - Rx xylitol, flax seed oil, copious fluid intake to minimize
- **Dysgeusia**
  - Counseling patient to avoid minimized PO intake (if no PEG/NGT)
- **Dermatitis**
  - Ensure proper skin/wound care and analgesia
- **Labs Abnormalities**
  - Monitor electrolytes if decreased PO intake and/or chemotherapy. Monitor CBC if chemotherapy.
Case: Follow-Up

- H&P + complete H&N physical exam +/- FOL
  - q1-3 months for year 1
  - q2-6 months for year 2
  - q4-8 months for years 3–5
  - Yearly for years > 5

- Baseline post-op CT at 3 months adjuvant treatment
  - Additional imaging practices vary per institution or as indicated by symptoms/exam

- TSH yearly (if thyroid irradiated)

- Speech/swallowing/dental/hearing evaluations

- Smoking cessation

- Depression screening
Oral Cavity Cancer: Clinical Pearls

• What is the ideal regimen of concurrent cisplatin?
  
  • Noronha et al, JCO 2018:
    - n=300 patients with LAHNC (87% oral cavity, 93% PORT)
  
  • Randomized:
    - Weekly cisplatin 30 mg/m²
    - Q3 Week 100 mg/m²
    - As administered with RT delivered by opposed portals
  
  • Caveats: Treatment and patient characteristics differ versus typical USA patients/practices; suboptimal dosing for weekly cisplatin (30 mg/m² rather than 40 mg/m²)
  
  • OCAT Trial (Laskar et al, ASCO 2016): Conventional RT (56-60 Gy/6 wk) vs CRT (56-60 Gy/6 wk + weekly cisplatin 30 mg/m²) vs Accelerated RT (56-60 Gy/5 wk) for high-risk oral cavity patients → showed similar locoregional control for all three arms

Improved LRC with Q3 week cisplatin but with more toxicity; no difference in OS
References

2. NCCN: Clinical Practice Guideline Head and Neck Cancers.

Please provide feedback regarding this case or other ARROcases to arrocase@gmail.com