Oropharyngeal Cancer

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The James Cancer Hospital and Solove Research Institute

<table>
<thead>
<tr>
<th>Relevance</th>
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<tbody>
<tr>
<td>• Rising Incidence of Oropharynx Cancer</td>
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<td>• HPV epidemic: Face of Head and Neck Cancer has changed</td>
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<td>• Many patients with oropharynx cancer present to their PCP with a neck mass</td>
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<td>• HPV vaccine: a unique opportunity to prevent oropharynx cancer</td>
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<table>
<thead>
<tr>
<th>Etiology</th>
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<td>• Smoking</td>
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<td>• EtOH</td>
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<td>• Immunosuppression</td>
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<tr>
<td>• Human Papillomavirus (HPV)</td>
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The Oropharynx
The HPV Era

• Despite declining prevalence of larynx, oral cavity cancer, oropharynx cancer on the rise

Typical Presentation of HPV-related oropharyngeal cancer

• Patients tend to be younger.
• Are more likely to be males, married and college-educated.
• Typically present without a significant history of tobacco or alcohol abuse.
• Have sexual risk factors for oral or genital HPV exposure.
• Present with low T and high N stage tumors.
• Usually non-keratinizing, poorly-differentiated, and of basaloid morphology on Histology.

HPV

• ds-DNA virus that infects skin and mucosa
• Low-risk: HPV-6 and 11
• High-risk: HPV-16 and 18
  – Associated with oropharyngeal cancers
• Viral oncogenesis: HPV proteins E6 and E7 degrade p53 and retinoblastoma protein, respectively

HPV

• Transmission through intimate contact with an infected partner
• Majority of sexually active population will have at least one HPV infection in their lifetime
• Infections are asymptomatic
• In most cases, oral infection clears without intervention within 1 year
**HPV-Related Oropharynx Cancer**

- Oropharyngeal SCC (OPSCC) in which HPV is detectable within the tumor
- Incidence of oral cavity cancer, larynx cancer, on the decline
- Incidence of oropharynx cancer has been increasing the past 20 years
- 70-90% of new oropharynx cancers are HPV related

**HPV-Related OPSCC**

- Smaller primary tumors
- Large, cystic neck metastases
- Cystic neck mass in an adult should be considered metastatic HPV-related OPSCC until proven otherwise

**HPV and OPSCC**

- No screening test for oral HPV infection
- Clinical significance of HPV infection unknown, most infections clear spontaneously
- Treatment and surveillance for HPV + and HPV negative oropharynx cancers are similar
  - Clinical trials underway for treatment de-intensification in HPV+ cancers

**HPV Vaccines**

- Universal efficacy of >90% for prevention of premalignant cervical lesions
- Limited data on prevention of oral HPV infection and OPSCC
- Prophylactic vaccine intended to prevent acquisition of virus prior to exposure
- Recommended for boys and girls ages 9 to 12 years, up to age 26
Top five reasons for not vaccinating adolescents

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percent of girls (%)</th>
<th>Percent of parents (%)</th>
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<tbody>
<tr>
<td>Lack of knowledge</td>
<td>19.1</td>
<td>22.8</td>
</tr>
<tr>
<td>Not needed or not indicated</td>
<td>14.7</td>
<td>10.0</td>
</tr>
<tr>
<td>Not recommended C</td>
<td>17.2</td>
<td>17.1</td>
</tr>
<tr>
<td>Not recommended C2</td>
<td>13.6</td>
<td>13.5</td>
</tr>
<tr>
<td>Not available online</td>
<td>11.5</td>
<td>11.8</td>
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Analysis of provider records showed that if HPV vaccine had been administered at health care encounters when other recommended vaccines were administered, ≥1 HPV vaccination coverage by age 13 years for the most recent birth cohort of girls could have been as high as 91%.

MMWR July 25, 2014 - CDC

Workup

- History
- Physical Examination
- Flexible Laryngoscopy
- Imaging: CT, PET/CT
- Tissue obtained for pathologic diagnosis and HPV studies

Early Stage Disease: T1-2, N0-1

1. Primary surgery (transoral or open resection, neck dissection)
2. Definitive Radiation Treatment
3. The third option of RT plus systemic therapy is only appropriate for T2, N1 (category 2B recommendation, >50% but <85% NCCN panel agreement)
   - Adjunt CRT is recommended (category 1) for adverse pathological features: Extracapsular nodal spread or positive mucosal margins

Locally or Regionally Advanced Resectable Disease: T3-4a, N0-1 or any T, N2-3

Consider enrollment in multimodality trials
1. CRT with high-dose cisplatin (category 1 for agent).
2. Transoral or open resection of primary and neck with appropriate adjuvant therapy: CRT or RT.
3. Induction chemotherapy followed by RT or CRT (category 3 recommendation - less than 25% of panel members agree that this is appropriate)
**Very Advanced Cancer**

Newly diagnosed locally advanced T4b (M0), unresectable nodal disease, patients unfit for surgery.

For patients with PS 0 or 1.

1. CRT with high-dose platinum as preferred agent (category 1), but other category 1 options include carboplatin/5-FU or cetuximab.
2. Induction chemotherapy followed by RT of CRT (category 3 recommendation).

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**Summary of Treatment Options for OPSCC**

<table>
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<th>Early Stage</th>
<th>Advanced Stage</th>
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<td>T1-2, N0-1</td>
<td>T3-4a, N1-2</td>
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- Organ Preservation Surgery (TORS) +/− XRT
- Concurrent CRT (T2N1)
- Induction chemotherapy followed by CRT
- Salvage Surgery with reconstruction

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**Case #1**

- 49 year old M presents for evaluation of a left tonsil ulcer
- Left otalgia x 3 months, occasional hemoptysis
- Never smoker
- No neck mass, no other symptoms
- No significant medical history

**Physical examination**

- Firm, 2 cm ulcer on the inferior pole of left tonsil. Lesion is within the left tonsil and does not involve the tongue base
- No palpable adenopathy
- Biopsy of left tonsil: HPV+ squamous cell carcinoma
- CT Neck and Chest: No regional or distant metastasis

- T1 N0 M0 HPV+ SCC Left Tonsil
Treatment Options?

• Early Tonsil Cancer, HPV+, Non-smoker
• Many good options:
  Surgical: Transoral robotic tonsillectomy, selective neck dissection, possible adjuvant tx
• Nonsurgical: Radiation treatment

Multidisciplinary Tumor Board Discussion

• Head and Neck Surgeons
• Head and Neck Radiation Oncology
• Neuroradiology
• Head and Neck Pathologists

Transoral Robotic Surgery

Final Pathology

• Squamous cell carcinoma, HPV+
• Clear margins
• No perineural or perivascular invasion
• 35 lymph nodes, negative for carcinoma
• Pt treated with surgery alone, no indication for adjuvant radiation treatment
**Case #2**

- 46 year old F presents a left neck mass
  - No smoking history
  - No symptoms
  - Present x 2 months
  - Slow growing
  - No notable past medical history

**Physical Exam**

- 3 cm, firm, mobile left level II lymph node
- No other palpable adenopathy
- Head and neck examination otherwise unremarkable
- Cranial nerves exam WNL

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**Flexible Laryngoscopy**

- [Image 57x142 to 297x321]
- [Image 317x142 to 556x321]
Flexible Laryngoscopy

- Fine needle aspiration: squamous cell carcinoma, HPV positive
- Diagnosis: Tx N2a Mx SCC Left neck, unknown primary

T1 MRI

Carcinoma of Unknown Primary

- Presentation of metastatic neck lymphadenopathy without the identification of a primary mucosal lesion
- Diagnosis of exclusion, depends on the diligence exercised in search for primary tumor
Unknown Primary Workup

• Clinical Examination

• PET/CT: May identify 37% of occult primaries

• Directed Biopsies:
  – Direct laryngoscopy, panendoscopy, transoral robotic palatine and lingual tonsillectomy
T1 N2a M0 HPV+ SCC Tonsil

- Nonsurgical
  - Concurrent chemoradiation

- Surgical
  - Transoral robotic surgery, left selective neck dissection
  - Adjuvant radiation treatment, possible adjuvant chemoradiation treatment

Case #3

- 40 yo M presents for evaluation of a right neck mass
  - Never smoker
  - No medical history
  - Asymptomatic
  - Present x 2-3 months

CT Neck
**PET/CT**

**Workup**
- Panendoscopy: No primary identified
- Bilateral Tonsillectomy
- Right tonsil: HPV+ Squamous cell carcinoma – 1.9 x 1.5 cm
- T1 N2b M0 HPV+ OPSCC

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**Chemoradiation Treatment**
- Concurrent cisplatin + Intensity modulated radiation treatment
- 5 days/week, 7 weeks treatment
- PET/CT, 12 weeks after completion of treatment for assessment of response

**Post-Treatment PET/CT**
**Post-Treatment Decision Making**

- Clinical exam: No visible lesion in the right tonsil
- Palpable right level II neck mass
- Tumor board recommendation:
  - Directed biopsies of right tonsil
  - Right selective neck dissection

**OR**

- Directed biopsies of right tonsil
  - Benign squamous mucosa, no carcinoma

- Right selective neck dissection
  - Matted lymph nodes with extensive necrosis
  - No viable tumor
  - No evidence of squamous cell carcinoma

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**Oropharynx Cancer: Summary**

- Incidence is on the rise
- HPV has changed the face of OPSCC
- HPV related tumors have better prognosis
- Many successful treatment options, multidisciplinary decision making
- Cystic neck mass in adult: HPV-related OPSCC until proven otherwise
- Vaccination may reduce OPSCC in future generations