Oropharyngeal Cancer

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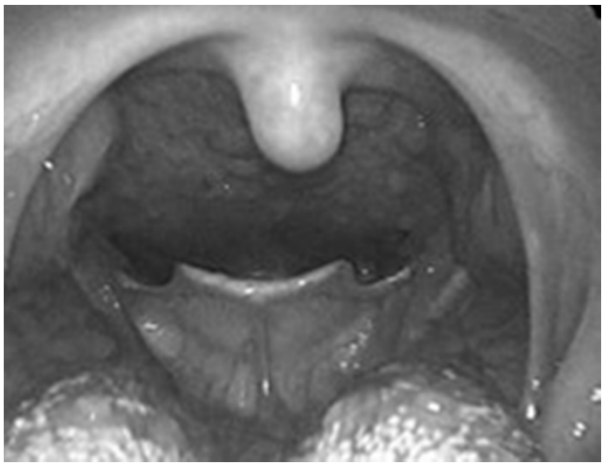
Relevance

- **Rising Incidence of Oropharynx Cancer**
- **HPV epidemic: Face of Head and Neck Cancer has changed**
- **Many patients with oropharynx cancer present to their PCP with a neck mass**
- **HPV vaccine: a unique opportunity to prevent oropharynx cancer**

The Oropharynx



Etiology

- **Smoking**
- **EtOH**
- **Immunosuppression**
- **Human Papillomavirus (HPV)**

The HPV Era

- **Despite declining prevalence of larynx, oral cavity cancer, <u>oropharynx cancer on the rise</u>**

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 2. Top five reasons for not vaccinating adolescents with human papillomavirus (HPV) vaccine* — National Immunization Survey-Teen, United States, 2013

Parents of girls			Parents of boys		
Reason	%	(95% CI)	Reason	%	(95% CI)
Lack of knowledge	15.5	(13.0–18.5)	Not recommended	22.8	(20.6–25.0)
Not needed or necessary	14.7	(12.5–17.3)	Not needed or necessary	17.9	(15.9–20.1)
Safety concern/Side effects	14.2	(11.8–16.8)	Lack of knowledge	15.5	(13.7–17.6)
Not recommended	13.0	(10.8–15.5)	Not sexually active	7.7	(6.4–9.2)
Not sexually active	11.3	(9.1–13.9)	Safety concern/Side effects	6.9	(5.6–8.5)

Abbreviation: CI = confidence interval.
* Analysis limited to parents reporting that they were not likely to seek HPV vaccination for their teen in the next 12 months or were unsure of their HPV vaccination plans.

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)***

- ***Adjuvant 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)**

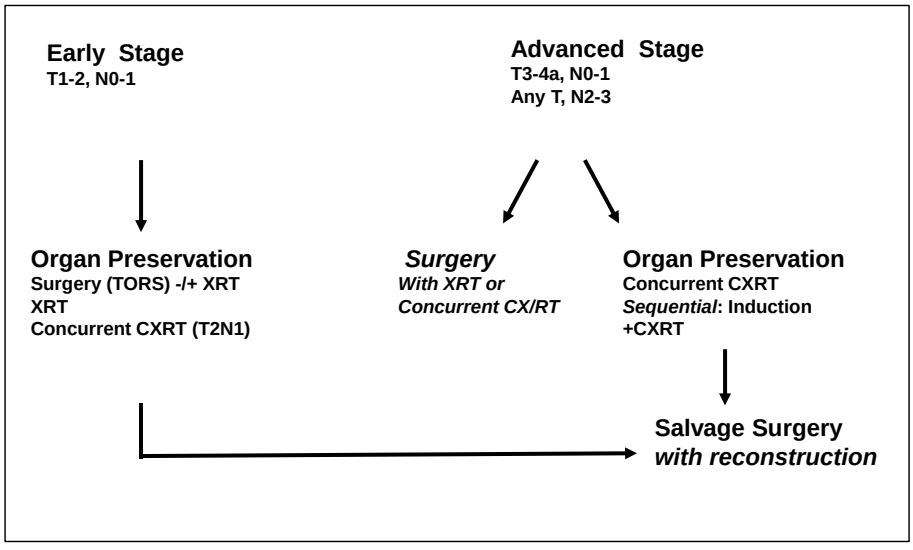
Very Advanced Cancer

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).**

Summary of Treatment Options for OPSCC



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**

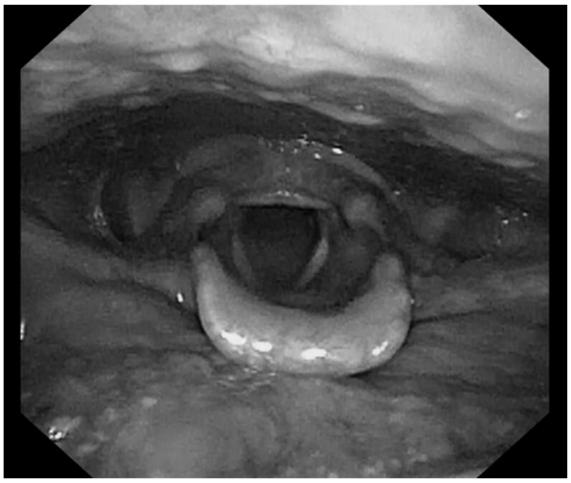
Case #2

- 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

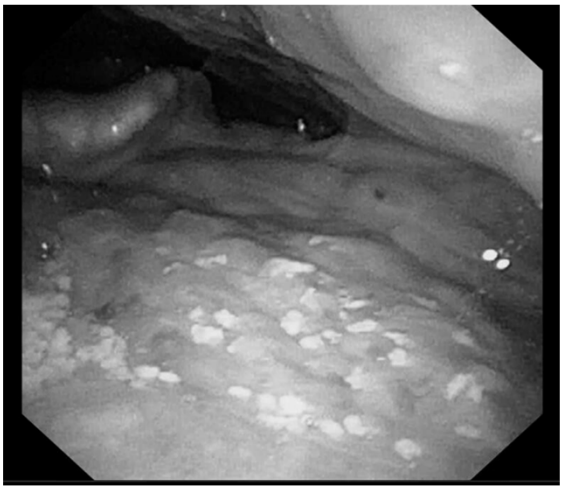
Physical Exam

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

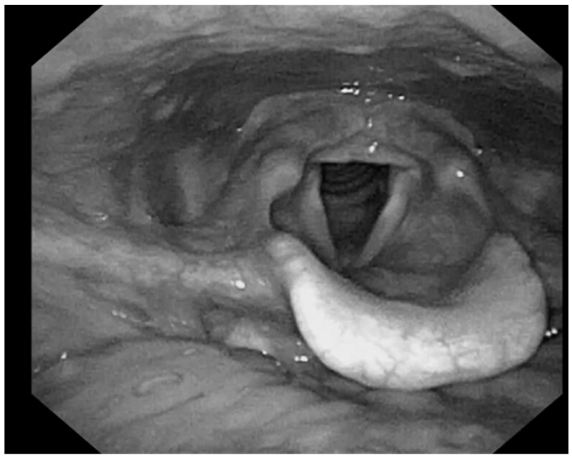
Flexible Laryngoscopy



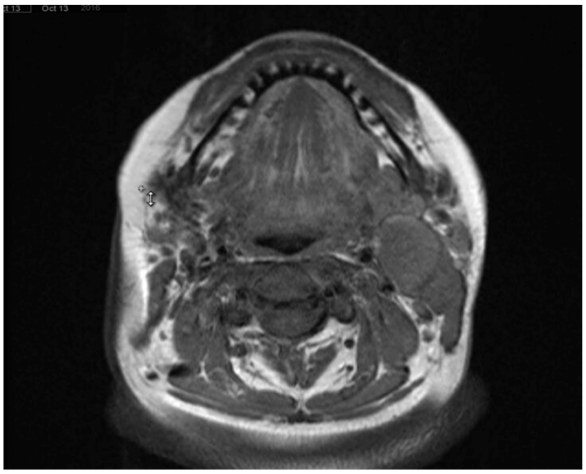
Flexible Laryngoscopy



Flexible Laryngoscopy



T1 MRI



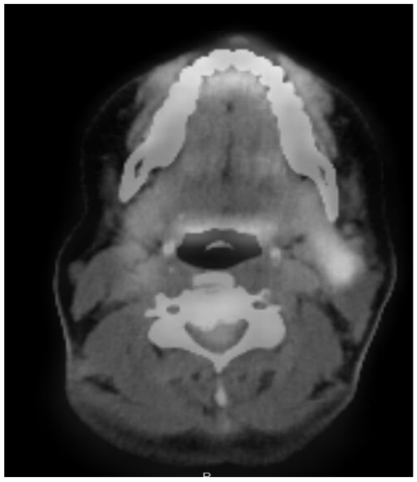
- **Fine needle aspiration: squamous cell carcinoma, HPV positive**
- **Diagnosis: Tx N2a Mx SCC Left neck, unknown primary**

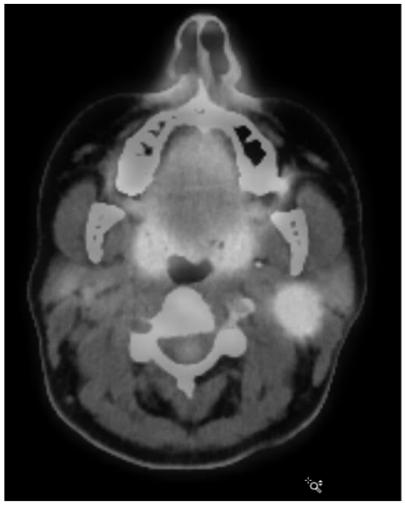
Carcinoma of Unknown Primary

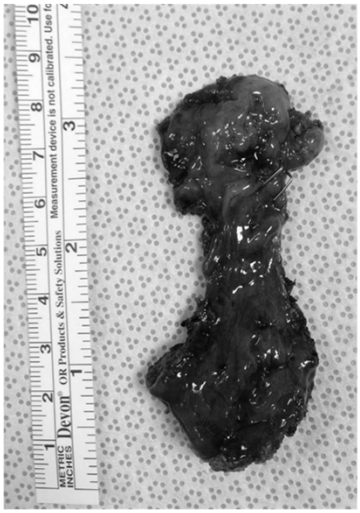
- **Presentation of metastatic neck lymphadenopathy without the identification of a primary mucosal lesion**
- **Diagnosis of exclusion, depends on the diligence exercised in search for primary tumor**

Unknown Primary Workup

- **Clinical Examination**
- **PET/CT: May identify 37% of occult primaries**
- **Directed Biopsies:**
  - **Direct laryngoscopy, panendoscopy, transoral robotic palatine and lingual tonsillectomy**







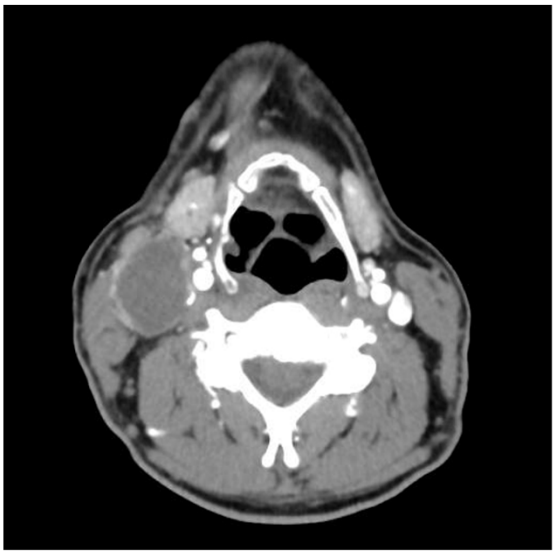
T1 N2a M0 HPV+ SCC Tonsil

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

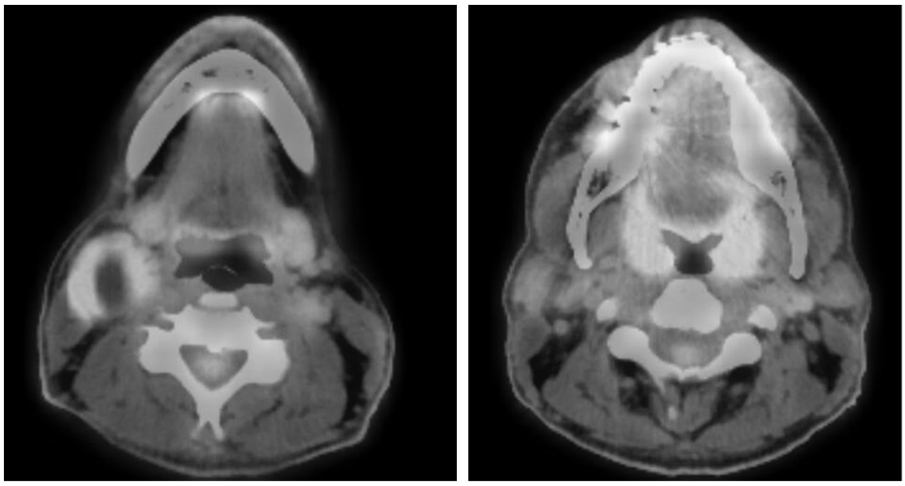
Case #3

- **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



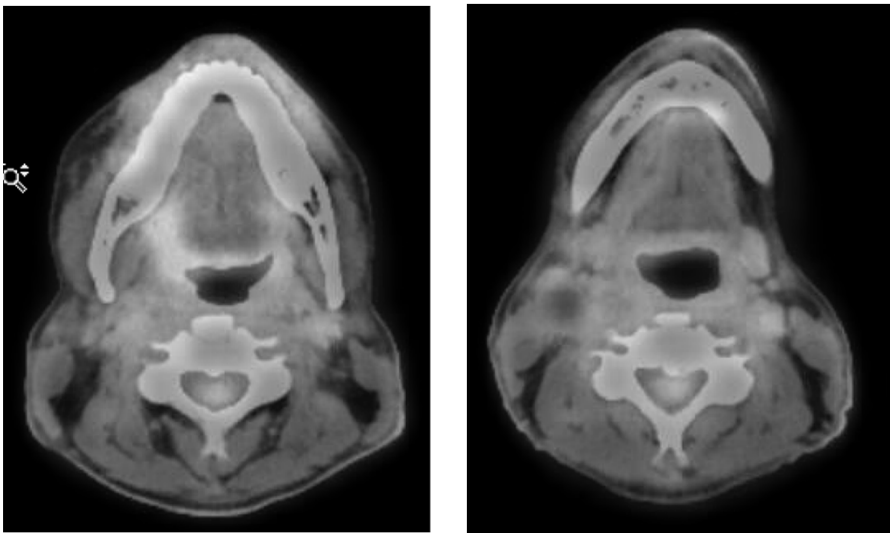
Workup

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

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

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**