HPV related Head and Neck Cancer

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Disclosure

•No conflicts of interest to disclose

Learning Objectives

1. Understand risk factors for Oropharyngeal Cancer (OPC)
2. Identify the clinical presentation of Oropharyngeal Cancer (OPC)
3. Become informed regarding the prevention of Oropharyngeal Cancer (OPC)
4. Be aware of treatment options for Oropharyngeal Cancer (OPC)

How HPV is Changing the Landscape of Head and Neck Cancer

Introduction

- 2 major factors have changed the profile and demographic of the “typical” head and neck cancer patient in North America
- The reduction in smoking has resulted in a lower incidence of laryngeal and hypopharyngeal SCC
- The widespread prevalence of HPV has resulted in a significant rise in the incidence of HPV-related oropharyngeal cancer (Tonsil, Base of tongue, soft palate)

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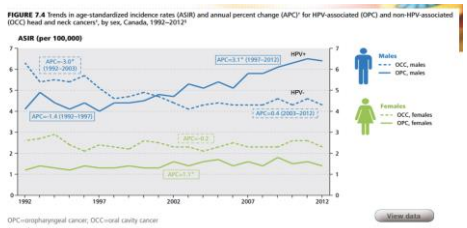

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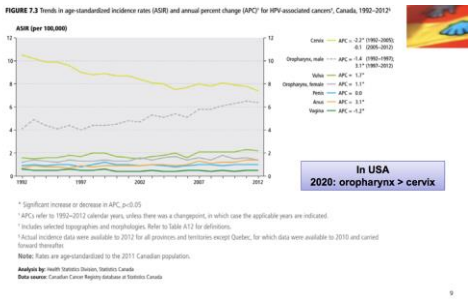

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Introduction

- 70 -80 % of all Oropharyngeal SCC is HPV in origin
- These patients are often NOT smokers, do not abuse ETOH, are middle age males and are from higher, more educated socio-economic backgrounds
- Due to the above, the index of suspicion when such a patient presents with a sore throat or a neck mass, might be inappropriately low

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Introduction

Primary care providers must keep this diagnosis in mind when the potentially "New Type" of head and neck cancer patient walks through their door

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HPV related Head and Neck Cancer
Case Study

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History

- Gary, a 55-year-old Caucasian investment banker presents with a large neck mass located in the upper neck (level 2) on the left side.
- Enlarging lump first noticed several months ago but demanding work life prevented primary care visit.
- Associated symptoms include persistent mild throat pain, moderate unilateral referred ear pain and occasionally tasting blood. He denies any symptoms of infection.
- Gary has never smoked and rarely drinks.

Physical Exam

- Non-tender, partly fixed, rubbery left sided upper neck mass measuring approximately 30-40mm.
- Very subtle left palatine tonsillar mass noted ~5mm. Lesion indurated and hard on palpation. Very scant bleeding from lesion when palpated.
- The rest of the HEENT exam is normal.

Investigations

- Bloodwork – WBC (? Infection e.g. infectious mononucleosis), TSH (thyroid origin).
- Fiberoptic nasopharyngolaryngoscopy - allows better visualization of the base of the tongue, the inferior aspect of the tonsils, the hypopharynx and larynx.
- U/S – evaluate neck mass and surrounding lymph nodes.
- Other: FNA biopsy and HPV immunohistochemistry, CT, FDG PET/CT, Panendoscopy.

Diagnosis & Management

•Gary's biopsy results confirm his diagnosis of HPV (p16 +) oropharyngeal squamous cell carcinoma with unilateral upper neck metastases.

•Management is dependent on the clinical staging and clinical context and is best handled by a multidisciplinary team.

Actual Case # 2

- ID- 57 yr old Male Corporate CEO
- CC- 4 week history of a sore throat
- Social Hx- Never smoked, very occasional social ETOH consumption
- PMH- Nil

Actual Case # 2

- HPI- 4 weeks of slowly escalating Lt sided sore throat, otherwise felt well
- P/E- Obvious swelling of left tonsil, no ulceration. Left tonsil was firm on palpation, with the induration extending into the soft palate. No palpable adenopathy

Actual Case # 2

- Biopsy tonsil- P16 + SCC
- CT- Confirmed the Left oropharyngeal mass and the absence of suspicious neck nodes
- Stage- T3N0M0

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Actual Case # 2

- Treatment- He was enrolled in a clinical trial and received 3 cycles of neo-adjuvant cis-platinum and taxotere, followed by planned Transoral Robotic Radical Tonsillectomy (TORS) and Left Neck Dissection
- He is Radiologically confirmed disease free 14 mths post treatment

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Actual Case # 3

- ID- 65 yr old Male Office Worker
- CC- Complains of a 1 yr hx of a slowly growing Rt neck mass, 3 wks of a Rt sided sore throat
- Social Hx- Never smoked, Does not consume ETOH
- PMH- Asthma

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Actual Case # 3

- HPI- 1 yr of a slowly growing Rt upper neck mass and 3 wks of escalating Rt throat pain
- P/E- Asymmetrical Rt tonsillar mass, 2 cm mobile Rt level 2 node, no other adenopathy
- Biopsy Rt Tonsil- P16 + SCC
- CT- Confirmed a Rt tonsil mass and a solitary Rt Jugulodigastric (Level 2) pathologic node

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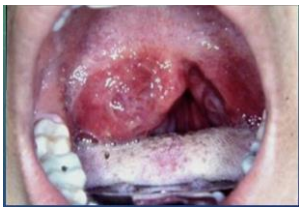

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Actual Case # 3- SO

- Stage- T1N1M0 Rt tonsil SCC
- Treatment- Enrolled in a clinical trial; was randomized to concomitant chemo/xrt

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Take Home Points

- 1) HPV Positive oropharyngeal ca is on the rapid rise
- 2) This is a “New Type” of head and neck cancer patient, typically middle aged, more educated and affluent adults (Males > Females). Often lack a smoking and ETOH history

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Take Home Points

- 3) Treatment options are many; and may include Robotic surgery, XRT and Chemo, in various combinations. Many clinical trials are ongoing to assess optimal treatment with best QOL outcomes
- 4) Prognosis is generally better than HPV negative oropharyngeal cancer

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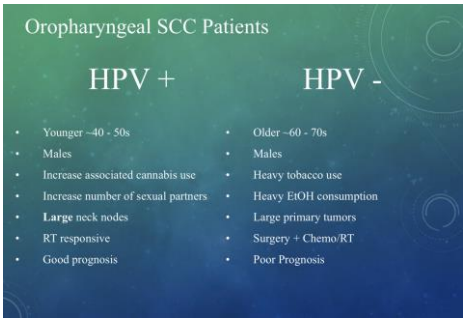

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HPV related Head and Neck Cancer
Management of a neck mass – Clinical Pearls

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Management of a neck mass - Clinical Pearls

- The presence of a persistent (3 weeks) neck mass in an adult over the age of 40 is most likely neoplastic until proven
- otherwise. While under the age of 40, etiology is weighted towards infectious/inflammatory.

All neck masses lasting more than 3 weeks should undergo ultrasound and be referred to an Otolaryngologist – Head and Neck Surgeon on a very urgent basis.

Management of a neck mass - Clinical Pearls

- The most common Head and Neck Cancers originate from:

1. Larynx - Vocal Cord, surprisingly low incidence neck metastases
2. Oropharynx - Palatine tonsil and base of tongue
   - Can be extremely small, non painful and almost invisible to detect
3. Oral Cavity - Floor of mouth
4. Lymph nodes themselves – lymphoma
5. Salivary gland cancer
6. Thyroid gland cancer

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Management of a neck mass - Clinical Pearls

- HPV is the newest leading cause of oropharyngeal cancer (OPC).
- HPV OPC usually presents at a more advanced stage and often the only presenting symptom is an isolated upper neck mass.
- Even in the absence of smoking, patients are at an increased risk of developing HPV OPC. Especially younger men (40-60 years).

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Treatment of HPV-Related Oropharyngeal Squamous Cell Carcinoma

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Case 4

- 69 yo male, referred for R neck mass x 2 mos
- Biopsy: SCCA P16+
- Underwent standard chemo/XRT
- 70 Gy in 35 fractions, using IMRT
- Concomitant Cisplatin
- Free of disease

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Case 4

- 58 yo male, film producer, referred with 3 mo hx asymptomatic L level II neck mass
- Non-smoker, social Etoh
- ENT exam: painless mass L BOT, Left adenopathy
- Biopsy BOT and FNA neck: SCCA, strongly P16+
- Stage T2N2b

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Case 4 Treatment Options

1. Standard chemo/XRT
2. Study: Chemo followed by Transoral Robotic Surgery (TORS)
- Patient chose option 2
- 1.5 yrs free of disease
- Swallowing well

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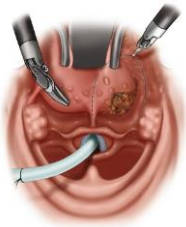
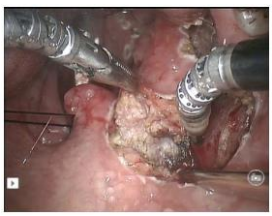
Transoral Robotic Surgery





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Why were these patients treated differently?

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Survival & stage

- HPV+: survival good for Stage I, II, III, and IVA disease
- HPV-: prognosis worsens with increasing stage of disease

❖*HPV+ OPC: better prognosis following relapse*
❖*Smoking mitigates the favorable effect of HPV+ OPC*

International Collaboration on Oropharyngeal Cancer Network for Staging study
Lancet Oncology 2016

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Stage & Survival by HPV Status

• HPV+	• HPV-
• Stage I: 88%	• Stage I: 76%
• Stage II: 82%	• Stage II: 68%
• Stage III: 84%	• Stage III: 53%
• Stage IVA: 81%	• Stage IVA: 45%
• Stage IVB: 60%	• Stage IVB: 34%

International Collaboration on Oropharyngeal Cancer Network for Staging study
Lancet Oncology 2016

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Emerging Trends

- HPV+ and HPV- tumors have different biology, prognosis
- 2017: separate TNM staging system for HPV+ and HPV- tumors better reflects prognosis

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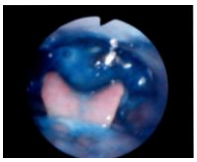
Current Standard Therapy

- Radiation, concurrent cisplatin
- Surgery for salvage
- Acute toxicity: mucositis, dysphagia, N&V, neutropenia, weight loss
- Late complications (progressive): dysphagia, aspiration, fibrosis, xerostomia, neck/shoulder stiffness, dental problems, osteoradionecrosis, hearing loss
- Many: permanent PEG/Trach
- Profound effect on QOL



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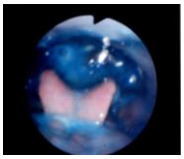
Current Standard Therapy

- Radiation with concurrent cisplatin
- Surgery for salvage
- Significant ***Acute*** toxicity ***and Late complications (progressive)***
- Many end up with permanent PEG/Trach
- Profound effect on QOL



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IS THERE A BETTER WAY?

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Prevention - Vaccination

- Quadrivalent vaccine covers HPV16 and 18
- 9-valent vaccine covers 6, 11, 16, 18, 31, 33, 45, 52, and 58

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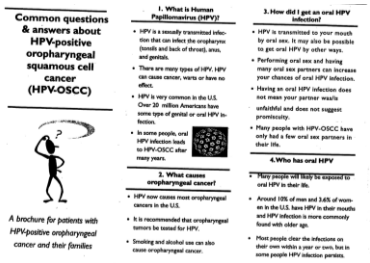
Education



Common questions & answers about HPV-positive oropharyngeal squamous cell cancer (HPV-OSCC)

A brochure for patients with HPV-positive oropharyngeal cancer and their families

1. What is Human Papillomavirus (HPV)?

2. What causes oropharyngeal cancer?

3. How did I get an oral HPV infection?

4. Who has oral HPV

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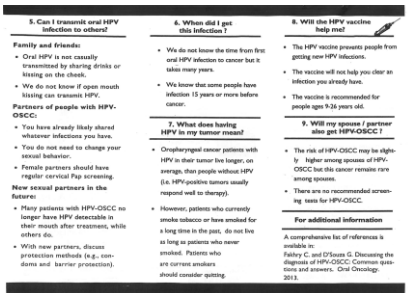
Education



5. Can I transmit oral HPV infection to others?

Family and friends:

- Oral HPV is not casually transmitted by sharing drinks or kissing on the cheek.
- We do not know if open mouth kissing can transmit HPV.

Partners of people with HPV-OSCC:

- You have already likely shared whatever infections you have.
- You do not need to change your sexual behavior.
- Female partners should have regular cervical Pap screening.

New sexual partners in the future:

- Many patients with HPV-OSCC no longer have HPV detectable in their mouth after treatment, while others do.
- With new partners, discuss protection methods (e.g., condoms and barrier protection).

6. When did I get this infection ?

- We do not know the time from first oral HPV infection to cancer but it takes many years.
- We know that some people have infection 15 years or more before cancer.

7. What does having HPV in my tumor mean?

- Oropharyngeal cancer patients with HPV in their tumor live longer, on average, than people without HPV (i.e. HPV-positive tumors usually respond well to therapy).
- However, patients who currently smoke tobacco or have smoked for a long time in the past, do not live as long as patients who never smoked. Patients who are current smokers should consider quitting.

8. Will the HPV vaccine help me?

- The HPV vaccine prevents people from getting new HPV infections.
- The vaccine will not help you clear an infection you already have.
- The vaccine is recommended for people ages 9-26 years old.

9. Will my spouse / partner also get HPV-OSCC ?

- The risk of HPV-OSCC may be slightly higher among spouses of HPV-OSCC but this cancer remains rare among spouses.
- There are no recommended screening tests for HPV-OSCC.

For additional information

A comprehensive list of references is available in:

Fakhry C. and D'Souza G. Discussing the diagnosis of HPV-OSCC: Common questions and answers. Oral Oncology. 2013.

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Clinical trials

- Current chemo/XRT protocol likely overtreatment
- Search for treatment with same excellent results with fewer acute/long term sequelae
- Ultimately: Improved function and QOL

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Clinical Trials: examples

1. Induction chemo followed by reduced XRT: 54Gy vs 70 Gy
2. XRT alone
3. TORS (surgery) with or without post-op XRT or chemo based on risk
4. NEC TORS trial: induction chemo followed by surgery

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Summary

- P16+ (HPV+) Oropharyngeal cancer has a very good prognosis, compared with P16- (HPV-) OPC
- Current chemo/XRT Rx associated with significant short/long term sequelae and compromised QOL
- Expect de-intensified protocols to emerge next few years
- Incidence expected to decrease with vaccination (as seen in laryngeal papillomas)

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