HPV and Head Neck Cancer

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Objectives

• Understand the role of HPV in oropharyngeal cancer
• Recognize the common clinical presentation
• Identify changing treatment paradigms
• Educate patients on screening and risk factors

Human Papilloma Virus (HPV)

• 100 types infect skin and moist surfaces
• Most common sexually transmitted infection
• 40 types that infect genital areas, mouth & throat
• Most infections are completely asymptomatic
• It is not a new virus or new type
HPV and Viral Oncology

- Cervical Cancer disease model
- Papanicolau (Pap) screening 1940s
- Hausen HPV DNA in cervical cancer 1970s
- HPV became implicated nearly all cervical cancers

Cervical Cancer Model

- Public health success
  - Risk factors were identified
  - Screening programs successful in secondary prevention
  - Primary prevention with HPV vaccination
  - Incidence and deaths decreased where screening/immunization
  - Learned nuances of the disease

Classic Oropharynx Cancer (OPC)

- Age 60-70s
- Smokers
- Drinkers
- Comorbidities
- Surgical morbidity
- Second primaries
Historic Oropharynx Cancer Survival

Evolution to a Non-Surgical Disease

• Open surgery and adjuvant RT/CRT until 1990s
• Pendulum swung to nonsurgical as trials showed good outcomes
  • Meta-Analysis of Chemotherapy on HN Cancer (MACH-NC): Concurrent CRT with 5% increase in OS at 5 years
• Intensification of non-surgical treatment with comparison to history surgical outcomes, RT alone as benchmarks

How Trials Helped

• Chemoradiation quickly became standard of care
• Determine who benefits from CRT
• High volume of oropharynx cancer
• RTOG trials 0129
  Decades of patients on trials with banked tissue, data on confounders
What Else Happened?

• Technology changed
• The disease changed
• Social habits changed
• Morbidity from aggressive treatment

Confirmation of HPV as a Risk Factor

First clear association of OP SCCA and HPV 16

Comparison of OPC to Controls

• Strong association between oral HPV infection and oropharyngeal cancer
• Sexual behaviors spread the virus to the oropharynx
• OP cancer significantly associated with
  – Oral HPV-16 infection (OR 14.6)
• Sexual activity associated with OP cancer
  – >25 vaginal partners (OR 3.1)
  – >5 oral sex partners (OR 3.4)
HPV & Malignant Cancer Risk

• 1-5 oral sex partners: Increased risk x2
• >6 oral sex partners: Increased risk x5

But
• Half of HPV-positive cancer patients have had 1-5 partners

Marur, Lancet Oncology 2010; 11:781-89

Percentage of Oropharyngeal Cancers that are HPV Positive

Chaturvedi AK, J Clin Oncol 2011; 29 (32): 4294-4301

Oropharyngeal Cancer Incidence 1998-2003

Male: 5700, Female 1300 per year in US

HPV Associated OPC

- Distinct clinical entity
- Majority of OP cancer cases
- Phenotype is small primary, cystic nodes
- Earlier onset 40-55 year olds, many are lifetime non-smokers
- Better prognosis
- Smoking still important

Best Evidence for Better Prognosis

- RTOG 0129
  - Stage III/IV HNC
  - Cisplatin with standard vs accelerated fractionation RT
  - Contemporary 2002-2005
  - Smoking history
  - 60% of the patients with OPC

HPV status was strong, independent prognostic factor for survival
Risk Stratification Based on HPV, Smoking, Tumor Size, and Nodal Size


3-yr OS

93%

71%

40%

HPV+, no tobacco

HPV+, > 10 pk year

HPV+, no tobacco

HPV negative

HPV Attributable Cancer 2006-2010

Division of Cancer Prevention and Control, CDC 2006-2010

HPV Associated OPC

CDC 2004-2008
Wisconsin Oropharynx Cancer Incidence Number of Reported Cases 1995-2011


HPV phenotype

Cystic Neck Masses: Missed Opportunities
Oropharynx Cancer: What next?

- New disease phenotype
- Generally better results with standard treatment
- Should approach to treatment change?
- Can treatment be de-intensified with same oncologic results?

Prospective Trials for HPV+ OPC

- Focus on de-intensification of treatment
  - Can less toxic chemotherapy be used?
    - RTOG 1016: Will substitution of cisplatin with cetuximab have comparable 5 year OS?
  - Can more chemotherapy be used to decrease RT?
    - Induction chemo to select 54 Gy vs 70Gy, (ECOG 1308)
  - Can surgery be used to avoid chemo, decrease RT?
    - ECOG 3311: Transoral surgery/ND with adjuvant therapy modified based on surgical findings
  - Can radiation alone achieve results; modest dose reduction?
    - HNO02: Weekly cisplatin/RT vs RT alone.
Patient Education

- Rapidly changing treatment paradigms
- Help navigate appropriate care
- Those whom de-escalation is not appropriate for:
  - Extensive smoking history
  - T4 disease
  - N2c disease

We will be a resource for questions related to HPV...
Questions about HPV: What is it?

- HPV is a sexually transmitted infection that can infect oropharynx, genitals, anus.
  - It is very common (~20 million Americans)
  - Many types (some cause warts)
  - Some people with oral infection will get OP cancer

Questions about HPV: How did I get it?

- HPV transmitted to mouth by oral sex
- Having more oral sex partners increases risk of oral HPV infection
- Many people who have HPV associated oropharyngeal cancer have had few sex partners

Questions about HPV: When did I get it?

- The time from HPV infection to cancer is many years (10-20 years)
- Most people with genital infections are asymptomatic
- The type that causes cancer does not have warts
- It does not mean that you/your partner was unfaithful
Questions about HPV: Why I get cancer from it?

- 20 million Americans have some type of HPV infection
- 10% of men; 4% of women have oral HPV infection
- Most clear within a year; some persist
- Small percentage get cancer

Questions about HPV: Can the cancer be spread?

- Do we need to change sexual behavior?
  - Not sure if kissing can transmit infection
  - Established partners have already been exposed
    - No need to change practices
    - OP cancer rare among spouses
  - New partners
    - Many with cancer with no active infection any longer

Questions about HPV: I was exposed to HPV. Can you screen me?

- There are no recommended screening tests currently for HPV.
- There is not a Pap equivalent.
- HPV vaccine prevents new HPV infection
- It will not help to clear any exposure*
- Offer exam and education.
- No role for tonsillectomy to date*
Prevention

- Clinical implications of remote tonsillectomy and risk of oropharynx cancer
  - Danish Cancer registry Fakry et al 2015
    - Tonsillectomy associated with decrease risk of tonsil cancer at age <60
    - Tonsillectomy associated with increased odd of base of tongue cancer and decrease odds tonsil cancer

- Prophylactic use
  - Posner et al. Role of Prophylactic Bilateral Tonsillectomy as a Cancer Preventive Strategy

Prophylactic Tonsillectomy: Need Better Risk Assessment

- Knowledge gaps
  - There is not a cancer risk prediction model
  - Biomarkers aren’t specific for site
  - No screening for premalignant lesions

  There is no current literature to support prophylactic tonsillectomy

Questions about HPV: Should kids really get that vaccine?

- Vaccination prevents infection with cancer causing types
- Rare opportunity to prevent cancer
- Important for boys and girls
- Data for safety, CDC
What can we do now?

- Primary prevention
  - Awareness, education re: oral sex
  - Vaccination for HPV
- Education & avoidance of missed opportunities
  - Good oral care, tobacco avoidance
- Continue to study the disease scientifically
  - Put patients on trials
- Advocate for patients to avoid overtreatment

Take Home Points

- Oropharyngeal cancer rates are increasing.
- Majority are associated with HPV infection.
- There is a specific phenotype (small primary, larger nodal burden) that mimics benign disease.
- HPV + OPC have better outcomes
- There are active trials assessing oncologic outcomes with less treatment.
- Otolaryngologist will need to educate patients and physicians about HPV