TAKE HOME POINTS

• The incidence of HPV-related oropharyngeal cancer has continued to rise
• It affects younger, healthier males
• The treatment of HPV-related oropharyngeal cancer continues to evolve
• Late effects of treatment can be devastating
• There is a presumption of immunization benefit

TRADITIONAL PRESENTATION OF HEAD AND NECK CANCERS

• Smoker-Drinker older male
• Painful mass, ulcer, nodule
• Change in longstanding leukoplakia
• Articulation change
• Otitis
• Bleeding
• Weight loss
• Dysphagia
• Airway obstruction with stridor
• Hoarseness
• Neck mass
CANCERS WITH RISING INCIDENCE
1999-2008
• Pancreas
• Liver
• Thyroid
• Kidney
• Melanoma
• Esophageal adenocarcinoma
• HPV-positive oropharynx

WISCONSIN OROPHARYNX CANCER INCIDENCE
CASES PER 100,000 1995-2011

ASSOCIATION BETWEEN ORAL HPV INFECTION AND OROPHARYNGEAL CANCER
• OP cancer significantly associated with
  • Oral HPV-16 infection (OR 14.6)
  • Seropositivity for the HPV-16 L1 capsid protein (OR 32.2)
  • Oral infection with any of 37 types of HPV (OR 12.3)

• Sexual activity associated with OP cancer
  • >25 vaginal partners (OR 3.1)
  • >5 oral sex partners (OR 3.4)

NATURAL HISTORY OF OROPHARYNGEAL CANCER
• Local invasion
• Regional metastases develop early
  - Bilateral
  - Levels II, III, IV, V

TRENDS IN HPV-POSITIVE AND HPV-NEGATIVE OROPHARYNGEAL CANCERS PER 100,000
HPV DETECTION BY SITE
CLINICAL PRESENTATION: OROPHARYNX CANCER

60 year-old competitive athlete

- Mild sore throat with enlarged tonsil. Small bilateral lymph nodes. Throat culture negative. Two courses of antibiotics. No resolution.
- Dental evaluation negative.

MANAGEMENT OF HPV-POSITIVE OROPHARYNGEAL CANCER

- Concurrent Platinum-based chemotherapy and radiation therapy
- Concurrent cetuximab and radiation therapy
- Surgery with postoperative radiation therapy
  - Transoral laser microsurgery (TLM)
  - Transoral Robotic Surgery (TORS)

SURGICAL APPROACHES

RADIATION APPROACHES

CHEMOTHERAPY AND IMMUNOTHERAPY APPROACHES

- Concurrent
- Neoadjuvant
- Cisplatin-based
- Cetuximab-based
- De-escalation trials
- Immune checkpoint inhibitors for recurrent cancer (pembrolizumab and nivolumab)
- Clinical trials (31 currently recruiting)

Overall Survival Based on Tumor HPV Status

**Risk Stratification Based on HPV, Smoking, Tumor Size, and Nodal Size**

- 3-yr OS
  - 93%
  - 71%
  - 46%

**PET Scan: Tumor Response**
April to October

**ETIOLOGIES AND ASSOCIATIONS – 2019**
- Tobacco
- Alcohol
- Human Papilloma Virus (especially HPV-16 and 18)
- Genetics
- Diet (Vitamin A, C, E)
- Dental irritation: poor oral hygiene
EXPECT MORE LONG-TERM SURVIVORS

- Age-adjusted limited-duration prevalence (LDP) of 5- and 10-year survivors by year of diagnosis

Huang SH, Refining AJCC/UICC Stage and PX Groups for HPV OC, J Clin Oncol 2015; 33:836-844

EXPECT MORE OROPHARYNGEAL SURVIVORS

- 5- and 10-year survivors by year of diagnosis

Patel MA, Cancer 2016; 122:1380-87

EXPECT MORE SECOND MALIGNANCIES

- Childhood Cancer Survivors Study (CCSS)
  - 14,358 individuals
  - 802 Second Malignant Neoplasms (SMNs)
  - 66 meningiomas
  - 1007 NMSC
  - 2.3-fold increase over seven year period
  - 20-year cumulative risk:
    - SMNs = 9.3%
    - NMSC = 6.9%
  - Highest risk groups: Female, Hodgkin’s or Sarcoma, Radiation

Patel MA, Cancer 2016; 122:1380-87

EXPECT CONTINUING CANCER DEATHS

- 35,958 three-year H/N cancer survivors (SEER)
- 13,120 deaths from any cause (5 years: 15%; 10 years: 41%)
- Leading causes of death:
  - HNSCC
  - SPMs
  - Lung 53%
  - Esophagus 10%
  - CRC 5%

Baxi SS, Cancer 2014; 120:1507-13

EXPECT DIFFERENCES IN RADIATION LATE EFFECTS

- Three-field technique
- Intensity Modulated Radiation Therapy (IMRT)
- 50 Gy @ 2 Gy/Fx
- 50 Gy @ 1.4 Gy/Fx

Shang Q, Applied Rad Onc. (9) 2015

EXPECTING SHIFTING CANCER TREATMENT EFFECTS

- Different late effect profiles between chemotherapy, EGFR agents, checkpoint inhibitors
- Financial toxicity
- Persistent HRQoL Effects
- Psychosocial support requirements

Rezzag EM, Cancer 2016; 122:1861-70
CASE REPORT: OROPHARYNX CANCER

60 year-old competitive athlete
2004 T2 N2c M0 oropharynx cancer treated with IMRT (70 Gy in 35 Fx) with weekly carboplatin and paclitaxel, then staged bilateral MNDs
2009 Dental deterioration, fibrosis, dyspnea on extreme exertion, mild dysphagia, vocal fold hypomobility
2011 Worsening fibrosis
2015 Increased mandibular swelling, ORN treated with HBO
2016 Spontaneous mandible fracture
- Biopsy: Osteosarcoma
- Doxorubicin and carboplatin x 2 cycles
- Hemimandibulectomy and fibula reconstruction

CDC ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

Recommended 9-valent HPV vaccine from ages 11 and 12 (can be given as young as 9) through age 45

DISEASES ASSOCIATED WITH HPV
- Oncogenic (high risk) types — e.g. HPV 16, 18
  - Cervix cancer
  - Vaginal cancer
  - Vulva cancer
  - Anus cancer
  - Anal cancer
- Non-oncogenic types — e.g. HPV 6, 11
  - Anogenital warts
  - Recurrent respiratory papillomatosis

TAKE HOME POINTS
HPV-RELATED HEAD AND NECK SCC OF THE OROPHARYNX
- Increasing in prevalence
- Often presents in men in their 50’s and 60’s
- Often presents with neck disease
- Associated with increased exposure to oral sex and increased number of partners
- MUCH better outcomes than non-HPV cancers
- Treatment options are evolving
- Encourage HPV immunization: “The Cancer Vaccine”

DO YOU RECOMMEND E-CIGARETTES? OR NOT?

Positives:
- Harm reduction
- Decreased combustible tobacco (98% of tobacco deaths)

Negatives:
- Dual use
- Has not been shown to help people quit
- Aerosol (not “vapor”) contains: nicotine, ultrafine particles, Benzene, Cadmium, Formaldehyde, Lead, Nickel, and Toluene

Source: CDC, Human Papillomavirus (HPV) for Clinicians: HPV: You Are the Key to Cancer Prevention. Page last updated: September 30, 2013: www.cdc.gov/HPV/YouAreTheKey/index.htm

Source: CDC, HPV Vaccination Rates of Adolescents, by State. Adolescents ages 13-17 with HPV Vp-2010 (US) Vaccination Service, 2017. 2017 US Average = 46.6%

Figure 4


Goniewicz ML, Tobacco Control March 6, 2013

E-CIGARETTES...

TOBACCO BY THE NUMBERS...

Tobacco use is the leading cause of preventable disease, disability, and death in the United States. Nearly 40 million US adults still smoke cigarettes, and about 4.7 million middle and high school students use at least one tobacco product, including e-cigarettes.

Cigarette smoking remains high among certain populations.
GLOBAL IMPACT OF TOBACCO

- 1.1 billion smokers worldwide
- 80% of smokers live in low- and middle-income countries (49% of men, 8% of women)
- 60% of smokers live in 10 countries (China, India, Indonesia, Russian Federation, US, Japan, Brazil, Bangladesh, Germany, Turkey)


Worldwide Cigarette Consumption and Lung Cancer Deaths

Worldwide Projected Smoking-Related Deaths

COMMENTS OR QUESTIONS

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