Head and Neck Cancers in the New Era

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HPV – What is it?

Some details about what HPV is and how it is typically contracted

- Human Papilloma Virus

- Most people infected with HPV will not have any symptoms and their immune system will get rid of the infection without any treatment.

- In some cases, however, HPV can lead to cancer.

- It's a minority that will lead to cancer, but clearly HPV can cause one.
HPV = Human Papillomavirus

HPV is a very common virus; nearly 80 million people—about one in four—are currently infected in the United States.

Most HPV infections don’t lead to cancer but certain types of HPV infection cause cancers. More than 100 varieties of human papillomavirus (HPV) exist.

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High and Low risk of HPV subtypes

Low-risk infection
Causes warts on the skin, mouth or genitals.

High-risk infection
Can lead to cancer
Cervical is the most common type of cancer caused by HPV.
It can also cause head and neck cancer in both men and women.
How is HPV Spread

- The skin or mucosa comes into contact with an infected person’s skin or mucosa.
- For high-risk HPV, this usually occurs through sexual contact.
- Most HPV infections that cause head and neck cancer are spread through oral sex, and possibly by “open mouth” kissing.

HPV – How it leads to Cancer

- Exposure to high-risk HPV infection
- Virus creates damage that eventually causes a tumor to grow. This process often takes many years.
- Most head and neck cancers that happen are a result of HPV infection occur in the part of the throat that includes the base of tongue and the tonsils.
HPVs infect basal cells of squamous epithelia through sites of mechanical trauma. Infections with high-risk HPVs can lead to dysplasia and carcinoma in situ and to invasive squamous cell carcinoma. Progression is a rare and slow process and many lesions regress spontaneously.
HPV – How is this Cancer Different?

- How it tumors grow differently
- Some details on why cancers of this type are easier to treat
  - Age difference
  - Younger patients
  - Healthier
- Diagnosis and Prognosis
  - HPV related cancers treatment outcome is far better and more curable vs when its related to tobacco and alcohol

HPV and Oropharyngeal Cancer

Latency from infection:

- Cervix (29 years) peak infection (20y) to cancer (49y)
- HPV (10-30y) peak infection (25-30 and 55-60) and cancer 58y
- HPV Vaccine impact expected by 2050
Gender differences

- Males more likely to be infected
  - ? Increased number of sexual partners
  - ? Differences in immunologic response
  - ? Cervical exposure
  - HPV 16
    - Cleared more slowly by males
Head and Neck: Squamous Cell Carcinoma

- 6th most common cancer worldwide (600,000 cases/yr)
  - 4% of malignancies in USA 52,500 cases/yr
- Oropharynx
  - 14,000 cases/year in USA
  - Males > Females 3:4:1
- Larynx
  - 12,000 cases/year
  - Alcohol/Tobacco
  - Male > Female 5:1 (formerly 15:1)

<table>
<thead>
<tr>
<th>HPV positive tumours</th>
<th>HPV negative tumours</th>
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</thead>
<tbody>
<tr>
<td>Anatomical site</td>
<td>ALL sites</td>
</tr>
<tr>
<td>Histology</td>
<td>Non-keratinised</td>
</tr>
<tr>
<td>Age</td>
<td>Younger cohorts</td>
</tr>
<tr>
<td>Sex ratio</td>
<td>3:1 men</td>
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<tr>
<td>Stage</td>
<td>T1, T1-2 Variable</td>
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<tr>
<td>Risk factors</td>
<td>Sexual behaviour</td>
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<tr>
<td>Incidence</td>
<td>Increasing</td>
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<tr>
<td>Survival</td>
<td>Improved</td>
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| Table 2: Differences between HPV positive and HPV negative head and neck squamous-cell carcinomas

Dramatic Rise in HPV + Tonsil Cancer

- HPV Most Common
- Smoking Less Common
The HPV-head and neck cancer link

- Retrospective analysis of 253 SCCa samples of head and neck
- 25% HPV positive (90% HPV-16)
- Oropharynx
- Poorly differentiated
- Less exposure to alcohol and tobacco exposure
- 59% reduced risk of death (vs HPV -)

Head and Neck Cancer – The Basics

- What anatomy is typically included and planned around in general
- Some general guidelines used
- Chains of nerves, fluids, and lymphatic systems
- What issues are there with irradiation in this region?

Oropharynx anatomy
Subsites of the Oropharynx

- Soft palate - Hyoid
- Posterior pharyngeal wall
- 2/3 of Waldeyer’s ring
- Tonsillar complex
  - *Tonsil, tonsillar fossa,
  - anterior and posterior tonsillar pillars
- *Base of tongue
  - Beyond circumvallate papillae
  - Visualization challenging

Cancers caused by HPV

- Cervix 100%
- Anal 95%
- **Oropharynx 70%**
- Vaginal 65%
- Vulva 50%
- Penis 5%

In the US, 3% of all cancers in women and 2% of all cancers in men

NIH NATIONAL CANCER INSTITUTE
Typical presentation

- Level II neck mass
- Minimal disease at "primary" site: tonsil or base of tongue
- Throat symptoms vague – Gobus
  - Pain uncommon
  - Difficulty swallowing is uncommon
  - Voice changes uncommon
  - Visible lesion may be absent

Robert Miller MD
www.aboutcancer.com
Watch the video at https://youtu.be/lSYagHQDjvY
Typical smoking related oropharynx cancer, presented with months of throat pain radiating into ear

In HPV + cancers the primary may be small and hard to see

Squamous Cell Carcinoma. This human papillomavirus-positive tumor presented as a diffuse erythroplakia of the left soft palate and tonsillar region.
HPV + Characteristics

- Neck mass
  - Cancer until proven otherwise in adults!!!
- Advance stage disease (3 or 4)
  - Nodal metastasis
  - Vague symptoms of primary site
- TNM findings
  - Small primary
  - Advanced nodal disease (cystic)

New ICON-S staging system was proposed for patients with HPV positive oropharyngeal cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>5 Year Survival</th>
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<tr>
<td>Stage I</td>
<td>T1-2N0-1</td>
<td>85-88%</td>
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<tr>
<td>Stage II</td>
<td>T3 or N2</td>
<td>78-81%</td>
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<tr>
<td>Stage III</td>
<td>T4 or N3</td>
<td>53-65%</td>
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</table>
Cervical lymph nodes

- 300 lymph nodes in the head and neck
- ~ 30 – 40% of total body lymphatics
- Embryological relation to venous system
- Mobile or Fixed?
- Tender to palpation?
- Change over time?

Oropharynx (base of tongue or tonsil)

- Tonsil
- Cancer
- Palate
- Uvula
- Tongue
The Optima trial- Head and Neck Treatment

- Low-risk patients with favorable response receive low dose 50 Gy radiation
- Low risk patients with moderate response (30%-50%) received low dose 45 Gy chemoradiation
- Low-risk patients with little to no response (>30%) received standard 75 Gy chemoradiation
- High-risk patients with favorable response received low-dose 45 Gy chemotherapy
- High-risk patients with favorable response receive standard 75 Gy chemoradiation

De- Escalation Trials for HPV…Can we use less chemotherapy or lower dose radiation and get the same result with less toxicity?
50 yo non-smoker, white male present with a lump in his left neck and the PET scan as noted

Typical Imaging for HPV Oropharynx Cancer

CT = large cystic node metastases  PET = large neck mass with small primary in tonsil
CT Scan Typical HPV + Patient

Large, Lobulated neck mass of lymph nodes with no obvious primary source

Neck biopsy = squamous

PET Scan Typical HPV + Patient

Large lymph node metastases in the neck with no obvious primary source
Stage IVA Squamous Cancer Left Base of Tongue, HPV +

Small cancer in left base of tongue

Large, necrotic lymph node mass

HPV Oropharynx Cancer

50 yo man, non-smoker presented with cystic neck nodes and occult primary in the base of tongue
HPV Oropharynx Cancer

53 yo man with large cystic neck node and occult primary in base of tongue

Typical Radiation Field for Cancer in Right Oropharynx

Part of the radiation includes the obvious cancer and other lymph node sites in the next but tries to spare normal structures like the parotid and brain
HPV Cancer – Head and Neck Planning Technique Walkthrough

Cumulative Dose Volume Histogram

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<tbody>
<tr>
<td>Parotid LR</td>
<td>Approved</td>
<td>100.00</td>
<td>14.3 cc</td>
<td>779.6 cGy</td>
<td>2165.3 cGy</td>
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<td>1310.2 cGy</td>
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<tr>
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<td>Spinal Cord</td>
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<td>32.6 cc</td>
<td>69.5 cGy</td>
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<tr>
<td>OAR</td>
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<td>30.5 cc</td>
<td>6669.7 cGy</td>
<td>17652.4 cGy</td>
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<td>Brain Stem</td>
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<td>6137.0 cGy</td>
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<td>575.3 cGy</td>
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<td>Brain PonsPVR</td>
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<td>Masticle</td>
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<td>3225.3 cGy</td>
<td>2794.6 cGy</td>
<td>1827.1 cGy</td>
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2018 Spring Regional Meeting
April 20 – 21, 2018
Denver/Downtown, Denver, CO
Max total dose 63Gy

Short Term Side Effects of Radiation to the Throat and Neck

1. Skin irritation
2. Dry Mouth and changes in taste and possible problems with teeth
3. Sore throat and problems with swallowing and dehydration and possible need for a feeding tube
4. Pain management problems
5. Laryngitis
6. Fatigue
Long Term Side Effects of Radiation to the Throat and Neck

1. The dryness may be permanent, depending on the amount of saliva glands in the field
2. Teeth may be vulnerable to decay, and caution is needed with future dental care to avoid jaw bone problems (osteonecrosis)
3. Problems with swallowing
4. Persistent hoarseness
5. Small risk of low thyroid
6. Carotid stenosis

Quick Response to Radiation combined with chemotherapy. Tonsil cancer gone by 2 ½ weeks

Squamous Tonsil Cancer  2.5 weeks after chemoradiation
Questions

Why You Should Worry about **HPV**