HPV-related anogenital cancers

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Outline

• HPV-related anogenital cancers
  • Cervical cancer
    • Precancerous cervical dysplasia
  • Vulvar and vaginal cancer
  • Penile cancer
  • Anal cancer

• HPV transmission and auto-inoculation
Cervical cancer

- Nearly 100% caused by HPV

Harald zur Hausen, Stockholm, 2008
Pathophysiology of HPV

Cervical Cancer

The Nobel Committee for Physiology or Medicine 2008
Illustration: Annika Röhl
Persistent HPV infection → Cancer

- HPV infection is necessary but not sufficient
  - Persistent infection occurs in 10-15%
  - Average time from infection → cancer is 15-25 years

- Risk factors for persistent HPV
  - Oncogenic, high risk subtypes
    - 16 and 18 cause 70-75% of all cervical cancer
  - Smoking
  - Compromised immunity
Cervical Cancer Diagnosis

- Mean age at diagnosis 48

- Symptoms
  - Irregular or heavy vaginal bleeding
  - Post-coital bleeding
  - Vaginal discharge
  - Abnormal pap smear

- In Wisconsin in 2012
  - 191 new cases
  - 54 deaths
Treatment and survival

- **Early stage cancer**
  - Stages IA1 to IB1
  - Surgery
    - Radical hysterectomy
    - Fertility sparing in some
  - 5 year survival 93%

- **Locally advanced cancer**
  - Stages IB2 to IVA
  - Chemoradiation
  - 5 year survival 15-80%
Cervical cancer incidence in WI, 1995-2011

Age adjusted incidence (per 100,000)

Wisconsin Cancer Reporting System, 2014
Progression of Pre-cancerous Cervical Dysplasia

- CIN 1
  - Represents acute HPV infection
  - Most will regress

- CIN 3
  - 30% will progress to cancer if untreated
Secondary Prevention of Cervical Cancer

- Pap smear screening
- 3 million abnormal paps/year in the US
  - Evaluation with follow up pap or colposcopy
Secondary Prevention of Cervical Cancer

- Management of cervical dysplasia
  - Low grade dysplasia $\rightarrow$ observe
  - High grade dysplasia $\rightarrow$ treat
    - Cryotherapy/LEEP/cold knife cone

- Adverse effects
  - Anxiety
  - Preterm labor risk
Other Genital Cancers in the US

PROPORTION OF CANCERS CAUSED BY HPV IN THE UNITED STATES

HPV infection causes virtually all cases of cervical cancer and a substantial proportion of several other cancers.

Other HPV-related genital cancers in women: vulvar and vaginal cancer
Vulvar cancer

- In Wisconsin (2012):
  - 90 cases
  - 30 deaths

- Symptoms
  - Itching
  - Visible lesion
Vaginal cancer

- In Wisconsin (2012)
  - 23 cases
  - 17 deaths

- Symptoms
  - Vaginal bleeding
  - Vaginal discharge
Vulvar and Vaginal Cancer Treatment

- Treatment
  - Surgical excision
  - +/- Chemoradiation
Incidence of vulvar and vaginal cancer in WI

Per 100,000 women, age adjusted

Wisconsin Cancer Reporting System, 2014
HPV-related cancer in men: Penile carcinoma
Penile cancer

- Usually presents in older men (> age 50)

- Symptoms
  - Painless
  - Lump, rash, or ulcer
  - Lymphadenopathy

- 30-35 cases/year in WI
Penile cancer

- 50% attributed to HPV
- Higher rates globally where there are high rates of cervical cancer
Anal cancer in men and women
Anal cancer diagnosis

- Symptoms
  - Rectal bleeding (45%)
  - Anal pain or sensation of mass (30%)
Anal cancer treatment and survival

- Most diagnosed early
  - Surgery +/- chemoradiation
  - 70% 5-year survival

- Advanced Stage
  - Chemoradiation
  - 19-59% 5-year survival
Progression of pre-cancerous anal dysplasia

- HPV infection $\rightarrow$

  $\rightarrow$ anal intraepithelial neoplasia (AIN 1 $\rightarrow$ 2 $\rightarrow$ 3) $\rightarrow$

  $\rightarrow$ anal cancer

- AIN 3
  - 8.5% risk of progression to cancer next 5 years

Rates of anal cancer

- 85-93% attributed to HPV
- Incidence increasing nationally and worldwide
  - Last 30 years in the US
    - 3-fold increase in men
    - 1.7 fold increase in women
- In Wisconsin (2012)
  - 107 cases
  - 17 deaths

Anal cancer incidence in WI

Age adjusted rate (per 100,000)

Wisconsin Cancer Reporting System, 2014
Transmission and auto-inoculation of HPV
Transmission of HPV

- Easily transmitted by **contact alone**
  - Skin to skin
  - Genital to genital
    - Condoms only 60% protection
  - Oral to genital
  - ? Oral to oral
Genital HPV transmission in couples

- Concordance of sexual partners 40-60%
- New couples
  - HPV rapidly transmitted to the other partner
- Usually both partners clear infections within 1-2 years

Oral autoinoculation

- NHANES 2010
  - 42.7% of women had cervical HPV
  - 3.8% of women had oral HPV

- Of those with cervical HPV, 5X > risk to have oral HPV also
  - ? autoinoculation of remote sites
  - ? oral to genital transmission

Autoinoculation of the anal canal

- Anal HPV prevalence in men
  - Up to 50% in MSM
  - Up to 17% in heterosexual males

- Anal HPV prevalence in women
  - Autoinoculation occurs after cervical infection
  - 50% have new anal HPV within 1 year of cervical infection

Stanley et al. HPV infection, anal intra-epithelial neoplasia (AIN) and anal cancer: current issues. BMC Cancer. 2012.
HPV Rates in the US

- 14 million new infections/year
- 79 million with current infection

At any given time in the US population
- 26.8-42.5% of the population has genital HPV
- About 7% has oral HPV

Lifetime risk > 80%

Dunne et al. JAMA. 2007; 297(8):813-819
Questions?

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