New insight in etiology and epidemiology of vulvar cancer

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No conflicts of interest
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After this presentation the participant will:
• Recognize risk factors for vulvar cancer
• Provide prevention strategies to reduce the risk for vulvar cancer
Vulvar Cancer

• Worldwide: incidence ~44,200; deaths ~15,200 in 2018

• US: accounts for ~ 3–5% of female genital cancers
  • 4th most common genital cancer – after uterine, ovarian, cervical
  • can occur on any part of the vulva but most often affects the clitoris, the inner edges of the labia majora, and the labia minora

Risk factors for vulvar cancer

- vulvar or cervical intraepithelial neoplasia
- history of cervical cancer
- cigarette smoking
- lichen sclerosus
- immunodeficiency syndromes
- northern European ancestry

Madsen BS et al. Int J Cancer 2008; Brinton LA et al. Gynecol Oncol 2017
Vulvar Cancer

• Majority ~75 to 90% of vulval cancers are squamous cell carcinoma (SCC). The next most common type is melanoma and accounts for 2 to 10%. Other rare vulval cancers are basal cell, Bartholin's gland cancer and extramammary Paget disease.
  • (Will therefore focus on SCC)

2 proposed pathways for the development of vulvar squamous cell carcinoma:

- HPV
  - Review of over 2000 specimens found HPV DNA ~87% HSIL/VIN, and 29% cancer (HPV 16 most common)

- Chronic inflammatory (vulvar dystrophy) or autoimmune processes (lichen sclerosus)
  - Differentiated VIN (dVIN) proposed as precursor lesion to cancer

dVIN and HSIL Oncogenesis

Normal Vulvar Epithelium
- Lichen Sclerosus
- Age, Immunity

dVIN
- Chronic oxidative genetic damage
- Genetics: p53, PTEN mutations, hypermethylation

Invasive Carcinoma
- Clone selection
- Therapy

Viral Factors:
- HPV type, load, persistence

Genetics:
p53, pRb, p21, p27 interaction
p16, Ki67 overexpression

Deregulated HPV E6-E7 oncoprotein expression in basal cells

VIN Usual type

INVASIVE CARCINOMA (Warty/Basaloid)

Apoptosis inhibition
- Aberrant proliferation
- Persistent telomerase activity
- Altered DNA repair process
- Aneuploidy
- Genomic instability
- Host immune system interaction

Therapy

Host Factors:
- Age, Immunity
- Smoking, Environment and Diet
- Sexual behavior

HPV clearance
Lesion regression

Fig. 1. Vulvar oncogenesis: Schematic representation of HPV-related pathway.
**HSIL Clinical Behavior**

**Progression to VSSC**
- ~5-6%

**Regression rate**
- ~1%
- < 35 years old or pregnant

**Risk Factors for progression**
- Immunosuppressed, smoking
- Advanced age, radiotherapy

**Lifelong risk**
- For recurrent HSIL
- For vulvar cancer

**Other screening**
- Pap with HPV

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Fig. 1. Vulvar oncogenesis: Schematic representation of HPV-related pathway.
dVIN Clinical Behavior

- Older Women: Postmenopausal
- More likely progression to VSSC: 32.8% dVIN vs 5.7% HSIL
- Progresses Faster: 22.8 mos vs 42.4 mos HSIL
- Treating LS (LP) reduces cancer risk

HSIL and dVIN

van de Nieuwenhof et al. Eur J CA 2009;851-56
Squamous Cell Cancer
Thank You!

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