Colposcopy of VIN and Vulvar Cancer
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Center for Vulvar Diseases

Learning Objectives

- To understand colposcopy of vulvar abnormalities
- To understand the neoplastic potential of VIN
- To recognize vulvar intraepithelial neoplasia and vulvar cancer
- To list the gross and colposcopic findings of VIN and vulvar cancer

Other Means of Magnification
Spalding Magnifiers Part 81-33-05 Toll free 1-888-855-8666
Local 713-466-3113
Houston, Texas.

Colposcopic Techniques

- 5% acetic Acid
- Soak initially for 3-5 minutes
- Use copious amounts
- Reapply often
- Avoid using in presence of breaks in epithelium or inflammation.

Other Solutions

- Lugol’s
  - Not useful (little glycogen present outside Hart’s line)

- Toluidine blue (1%)
  - Historic- stains normal tissue

Clinical Pitfalls of vulvar Colposcopy

- Acetowhitenings is nonspecific
- Normal anatomic variants- like vestibular micropapillae- often confused with HPV colposcopically and histologically
- Marked acetowhite changes in up to 65% of normal women.
Vulvar Biopsy Techniques

- **Anesthesia**
  - 1% xylocaine with or without epinephrine
  - 27-30 gauge needle to inject 1-3 cc’s of anesthetic agent
  - Inject subepidermally

- **Punch Biopsy**
  - Tischler cervical biopsy
  - Keyes punch
  + 3-5 mm diameter dermatologic instruments (usually 4 mm)

- Fine suture (3.0 or 4.0 Vicryl Rapide) vs. Monsel’s/ Silver nitrate

Condyloma

- Over 100 types of VPH
  - 30 are found on the genital area
- May cause itching, bleeding and occasionally pain

Intraepithelial Neoplastic Disorders of the Vulvar Skin and Mucosa

A. Squamous
  1. Vulvar intraepithelial neoplasia type 1 (VIN I)
     - mild dysplasia
  2. VIN II – moderate dysplasia
  3. VIN III – Severe dysplasia

B. Other
  1. Paget’s disease (intraepithelial)
  2. Melanoma in situ (level I)

*Classification system developed by the International Society for the Study of Vulvovaginal Diseases.

*ISSSUD 2003 new terminology

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
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<tbody>
<tr>
<td>1986</td>
<td></td>
</tr>
<tr>
<td>VIN 1</td>
<td>HPV effect</td>
</tr>
<tr>
<td>VIN 2</td>
<td>VIN</td>
</tr>
<tr>
<td>VIN 3</td>
<td>VIN</td>
</tr>
<tr>
<td>VIN 3</td>
<td>Differentiated VIN</td>
</tr>
<tr>
<td>Diff Type</td>
<td>- Unclassified VIN (NOS)</td>
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</table>
Incidence of Vulvar Intraepithelial Neoplasia (VIN)

- Incidence increasing
- Over the past 20 years, incidence has doubled, especially in women less than 40 years of age (50% of all cases)
- Progression to carcinoma appears to be uncommon in this age group, in the non-immunosuppressed patient.

Low grade VIN High grade VIN \( \rightarrow \) Risk of cancer

History of VIN III

- Before 1970, VIN was found most often in women in the fifth or sixth decade of life
  - Older women with VIN more often have solitary lesions with a higher risk for progression to cancer

Increasing Incidence of VIN

- Heightened awareness of neoplasia
- Increased tendency to perform biopsies
- Commonly associated with other lower genital tract neoplasia (anus, vagina, cervix) and/or carcinomas

Human Papillomavirus and VIN

- HPV 16 and 33 are the most common subtypes detected in VIN (90% of VIN lesions associated with these two types)
- 1/3 of patients with HPV are at risk for recurrence of disease after treatment

Risk Factors for VIN

| History of HPV (vulva, Vagina, cervix) | Immunosuppression |
| Early age of onset of Sexual intercourse | * Pregnancy |
| Multiple lifetime sexual Partners | * HIV |
| Cigarette smoking | * Autoimmune connective tissue disorders |
| * Diabetes |
| * Transplant recipient |
| * Cronic hepatitis |
| * Chemotherapy |
## Relationship of VIN to Various Factors

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
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<tbody>
<tr>
<td><strong>Age (y)</strong></td>
<td>35-65</td>
<td>55-85</td>
</tr>
<tr>
<td><strong>Condyloma history</strong></td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td><strong>STD history</strong></td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td><strong>Prior vulvar lesion</strong></td>
<td>VIN</td>
<td>LS, SCH</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>Basaloid</td>
<td>Keratinizing</td>
</tr>
<tr>
<td><strong>Cervical neoplasia</strong></td>
<td>High Presence</td>
<td>Low presence</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>High Presence</td>
<td>Low Presence</td>
</tr>
<tr>
<td><strong>HPV DNA</strong></td>
<td>Common</td>
<td>Seldom</td>
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</table>

### Vulvar Intraepithelial Neoplasia Squamous Type

- **VIN I**
  - < 1/3 mild dysplasia (formerly mild atypia) 40% of VIN (ICD9=624.8)
- **VIN II**
  - 1/3 to 2/3 moderate dysplasia (formerly moderate atypia) 14% of VIN (ICD9=624.8)
- **VIN III**
  - > 2/3 severe dysplasia (formerly severe atypia), (carcinoma in situ) 46% of VIN (ICD9=233.3)

*Es más alta la frecuencia de VPH en vulva que no es diagnosticada por ser infección subclínica.*

### VIN of low Grade: A Challenging Diagnosis

- Eur J Gynaecol Obstet 1994;15:70-4

#### VIN III

- **VIN III** (Squamous cell CIS, Bowen’s disease, Erythroplasia of Queyrat, CLS simplex)
Symptoms and Signs

- Most – completely asymptomatic
- Itching or burning
- Irritation
- Dyspareunia
- Labial erythema
- Patient notes a lesion

VIN

- Distribution
  - Most commonly found on the non-hairbearing areas
  - Posterior vulva and periclitorial area
  - May extend to involve the anus, vagina, clitoris, or urethra

VIN Lesions

- Unifocal or multifocal
  - White
  - Gray-brown
  - Red

Colposcopic Features of VIN

- Similar to but not as prominent as with CIN
  - Leukoplakia
  - Acetowhitening (70%)
  - Punctuation
  - Atypical vessels

VIN Thiickness

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>Depth (mm)</th>
<th></th>
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<tr>
<td></td>
<td></td>
<td>Deep</td>
<td>Shallow</td>
<td>Mean</td>
<td></td>
</tr>
<tr>
<td>Hairy skin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Labial majora</td>
<td>2085</td>
<td>1.04</td>
<td>0.08</td>
<td>0.37</td>
<td></td>
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<tr>
<td>Non-hairy skin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labial minora</td>
<td>945</td>
<td>0.86</td>
<td>0.11</td>
<td>0.38</td>
<td></td>
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<tr>
<td>Posterior fourchette</td>
<td>70</td>
<td>0.69</td>
<td>0.15</td>
<td>0.38</td>
<td></td>
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<tr>
<td>Perineum</td>
<td>195</td>
<td>0.85</td>
<td>0.11</td>
<td>0.47</td>
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</table>

**Anoscopy**

- Perianal involvement is noted in 33% of patients

**INSTRUMENTS**

- Hinkel-James Anoscope
- Fansler Operative Anoscope

**POSITIONS**

- Exaggerated Lithotomy Position
- Left Lateral or Sim’s Position
- Knee-Shoulder Position

**Non- squamous Types**

- Paget’s disease
- Melanoma in situ
Paget’s Disease

- Multifocal, Eczematoid red weeping area Brick red Scales, Eczematoid plaque Sharply demarcated border
  *Lesiones acetoblanca nítidas sobre mucosa eccematosas (enrojecida y humeda)*
- Occurs most commonly on the nipple and areola, where its presence signifies an underlying adenocarcinoma of the breast
- Apocrine gland origin
- Red velvety area with white islands of hyperkeratosis and at times may be pinkish, and eczematoid

**Paget’s Disease**

**Association with Adenocarcinoma**

- Genital
  - Vaginal, Cervical, Uterine
- Urologic
  - Urethre, Bladder
- Gastrointestinal
  - Anorectal, Rectal
- Breast

**Paget’s Disease**

**workup**

- History and PE
  - Symptoms include itching, burning
  - Signs include velvety appearance and bleeding
- Papanicolaou smear
- Mammogram
- Cystoscopy
- Colonoscopy

**Differentiating Paget’s From Other Conditions**

- Positive mucin as well as immunoperoxidase CEA staining can be used to differentiate
  Paget’s disease from melanoma
  - Paget’s (mucin and CEA positive)
  - Melanoma (mucin and CEA negative)
Paget’s Disease

- Paget’s Disease
  - Wide local excisión (how far?)
  - Margins
    + Extends beyond the visibly demarcated margin
    + Adequate surgical margins difficult to obtain
    + Local recurrence
      - 31% -radical vulvectomy
      - 43% wide local excision

Adenocarcinoma association as high as 26%

Melanoma in Situ
Melanoma in situ is a lesion of uncertain natural history, but it can be treated effectively with conservative surgery.

LS
VIN/ Vulvar Cancer
HPV

LS
VIN/ Vulvar Cancer
HPV
Human Cancer Viruses

<table>
<thead>
<tr>
<th>Virus</th>
<th>Cancer</th>
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<tbody>
<tr>
<td>Human papilloma virus (HPV)</td>
<td>Anogenital cancers</td>
</tr>
<tr>
<td>Hepatitis B virus (HBV)</td>
<td>Liver cancer</td>
</tr>
<tr>
<td>Epstein-Barr virus (EBV)</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Human T-cell lymphotropic virus (HTLV)</td>
<td>Adult T-cell leukemia</td>
</tr>
<tr>
<td>Kaposi’s sarcoma-associated herpes virus (KSHV)</td>
<td>Kaposi’s sarcoma</td>
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Cancer
Anogenital cancers
Liver cancer
Lymphoma
Adult T-cell leukemia
Kaposi’s sarcoma
Actions of Oncogenes

Growth factors
Intercellular signals
Gene expression
Receptors
Transcription factors
Growth control genes

(cell division)
M phase
G2 phase
G1 Phase
S phase
(DNA synthesis)

Human Cancer Viruses
Mechanisms of Action

<table>
<thead>
<tr>
<th>Virus</th>
<th>Mechanism</th>
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<tbody>
<tr>
<td>HPV</td>
<td>Inactivation of p53 and pRb</td>
</tr>
<tr>
<td>HBV</td>
<td>Liver damage - chronic proliferation</td>
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<tr>
<td>EBV</td>
<td>Immortalization - myc translocation</td>
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<tr>
<td>HTLV</td>
<td>Transactivation by viral tax protein</td>
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<tr>
<td>KSHV</td>
<td>Molecular piracy (IL-6, cyclin D, bcl-2)</td>
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Human cancer viruses mechanisms of action
Virus mechanism
HPV Inactivation of P53 and pRb
HBV Liver damage – chronic proliferation
EBV Immortalization- myc translocation
HTLV Transactivation by viral tax protein
KSHV Molecular piracy (IL-6, cyclin D, bcl-2)
P53 Damage Checkpoint Control
Damage to DNA - p53 - Inhibitor of Cdk-Cyclin – G1 Transition Blocked - S phase

Human Papillomavirus Proteins

**REPLICATION**
- E1 - *DNA Helicase*
- E2 - *Transcriptional Activator/Repressor*

**TRANSFORMATION**
- E6 - *Targets p53*
- E7 - *Targets Rb*
REPLICATION  E1- DNA Helicase
   E2- Transcriptional Activator/Repressor
TRANSFORMATION  E6- Targets p53
   E7- Targets Rb

References

HPV REFERENCES


VIN (Squamous and Nonsquamous) References


Fanning J, Lambert HC, Hale TM, Morris PC, Schuerch C. Paget’s disease of the vulva: prevalence of associated vulvar adenocarcinoma, invasive Pagetomas