Vulvar Carcinoma
Jacqueline Morgan
2/8/2017
A 72-year-old woman requests evaluation for chronic pruritis and soreness in the left labium majus. Self-application of talc and topical anti-fungal cream has not provided relief of her symptoms. Examination shows a 3-cm erythematous scaling patch on the inferior aspect of the left labium majus. The lesion is biopsied, and the histopathology is illustrated in the photograph.
Question 1

Which of the following is the most likely diagnosis?
- Dysplastic nevus
- Paget's disease
- Malignant melanoma
- Squamous cell carcinoma \textit{in situ} (CIS)

Which of the following is the most appropriate treatment for this patient?
- Wide local excision
- Topical 5-fluorouracil
- Simple left hemi-vulvectomy
- Radical local excision with left inguinal-femoral lymphadenectomy
A 70-year-old woman with infrequent gynecologic care is referred from the Primary Care Clinic for evaluation of a painful mass on the vulva. The patient mentions that she has had a long history of vulvar pruritis for which she has intermittently used over-the-counter antifungal agents. She first noted a small lump on the vulva approximately six months ago, but the discomfort has increased over the last three months. On examination, there was a 2.1 cm exophytic, erythematous lesion involving the medial aspect of the left labium majora. The remainder of the pelvic examination, including visual inspection and palpation, was negative. A biopsy was performed, and the histopathology is depicted in the photomicrographs, which demonstrate low-power (Figure 1) and high-power (Figure 2) images of the lesion.
Question 2

- Which of the following is the most likely diagnosis?
  - VIN 3
  - Squamous hyperplasia with atypia
  - Invasive squamous cell carcinoma
  - Melanoma

- Which of the following is the most appropriate treatment for this patient?
  - Simple vulvectomy
  - Radical vulvectomy with ipsilateral inguinal lymph node assessment
  - Radical vulvectomy with bilateral inguinal lymph node assessment
  - Radiation therapy
An 83-year-old woman requested evaluation because of vulvar pain. Physical examination showed a left vulvar lesion (Figure 1) and an enlarged left inguinal node. Biopsy of the vulvar lesion is shown in Figure 2.

Which of the following is the most likely diagnosis?
- Melanoma
- Adenocarcinoma
- Squamous cell carcinoma
- Sarcoma
Question 3

- Which of the following factors is most predictive of the patient's probability of survival?
  - Lesion size
  - Differentiation
  - Nodal spread
  - Tumor ploidy

- Which of the following is the most appropriate treatment for this patient?
  - Wide local excision
  - Modified radical vulvectomy
  - Modified radical vulvectomy and unilateral groin dissection
  - Modified radical vulvectomy and bilateral groin dissection
A 40-year-old homeless female was transported to the emergency room after being found unresponsive on a park bench. You are called to evaluate the patient's large vulvar mass (see illustration). When the patient is clinically stable and alert, you perform a biopsy of the mass. The preliminary pathology report is consistent with a sarcoma.
Question 4

Which of the following is the most common histologic type of vulvar sarcoma?

- Liposarcoma
- Angiosarcoma
- Epithelioid sarcoma
- Leiomyosarcoma

Which of the following is the usual treatment for a vulvar sarcoma?

- Radiation
- Wide surgical excision
- Chemotherapy
- Immunotherapy
Vulvar Cancer

- Encompasses Labia majora, minora, vestibule, clitorus
  (Down there, vagina, butt, *&##$, privates, %^$&)
- Epidermis, Apocrine and Bartholin glands, dermal tissue
From 2005-2009, the median age at diagnosis for cancer of the vulva was 68 years.

The age-adjusted incidence rate was 2.3 per 100,000 women per year.

From 2005-2009, the median age at death for cancer of the vulva was 79 years.
SEER Projection Data

- 0.27% of women born today will be diagnosed with cancer of the vulva at some time during their lifetime.
- OR
- 1 in 370 women will be diagnosed with cancer of the vulva during their lifetime.

2017 American Cancer Society’s estimates
- 6020 new cases
- 1150 deaths
Incidence

Rates are per 100,000 females and are age-adjusted to the 2000 U.S. standard population.

<table>
<thead>
<tr>
<th>Color</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light Blue</td>
<td>1.03 – 1.78</td>
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<tr>
<td>Medium Blue</td>
<td>1.78 – 2.11</td>
</tr>
<tr>
<td>Dark Blue</td>
<td>2.12 – 2.88</td>
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Incidence and Mortality
Age Related Incidence of Vulva Carcinoma
Vulvar Carcinoma

- Squamous Cell Carcinoma
- Melanoma
- Adenocarcinoma
- Sarcoma
- Basal Cell Carcinoma
- Verrucous
- Pagets
Presentation

- Variable
- Itching
- “Yeast infection”
- Burning
- Pain
- Bleeding Discharge
- Lump/Bump/Mass
- Often delayed over 6-12 months after symptoms arise
Evaluation

- History
- Examination
- Biopsy
  - Punch biopsy
  - Excisional biopsy
Differential Diagnosis

- VIN
- CIS
- Pagets
- Lichen sclerosus
- Vestibulitis
- Condyloma
- Herpes
- STIs
Melanoma

- <10% of vulva malignancies
- Changing pigmented lesion
- Bleeding
- Itching
Melanoma Staging

- Histologic Type
  - Superficial spreading
  - Mucosal Lentiginous
  - Nodular

- Staged as for other cutaneous melanomas
# Melanoma Staging

<table>
<thead>
<tr>
<th>Breslow</th>
<th>Clark’s Level</th>
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<tbody>
<tr>
<td>&lt;0.76mm</td>
<td>I- Intraepithelial</td>
</tr>
<tr>
<td>0.76-1.5mm</td>
<td>II- Into Papillary Dermis</td>
</tr>
<tr>
<td>1.51-2.25mm</td>
<td>III- Filling Papillary Dermis</td>
</tr>
<tr>
<td>2.26-3.0mm</td>
<td>IV- Into Reticular Dermis</td>
</tr>
<tr>
<td>&gt;3.0mm</td>
<td>V- Into Subcutaneous Fat</td>
</tr>
</tbody>
</table>
Melanoma Staging

- AJCC - TNM
- Tumor
  - Thickness
  - Mitotic Rate
  - Ulceration
- Nodal
  - Sentinel node assessment or Clinical
- Metastasis
  - LDH level
Melanoma Prognosis

- Poor
- Rising
- Older age patients
- Early distant spread

- 21% – 54% 5 yr survival
Melanoma Spread

- Lymphatic
- Hematogenous
Treatment- Surgery

- Surgical resection of lesion
- No benefit of radical vulvectomy over wide local resection- provided negative margins
- Lymph node assessment controversial
  - Will alter prognosis but not survival
Melanoma Treatment

- Chemotherapy
  - Multiple agents

- Immunotherapy
  - Interferon alpha
  - Interleukin 2

- Targeted therapy
  - Vemurafenib targets melanoma cells with the altered *BRAF* gene
  - *PD1* agent- *Nivolumab*
  - *MEK inhibitor*
  - *Anti CTLA4 antibodies*

- Radiation
  - Palliative
Bartolin Gland Carcinoma

- Adenocarcinoma
- Transitional Cell
- Adenosquamous
- Adenoid Cystic
- Neuroendocrine
Bartolin Gland Carcinoma

- Often initially misdiagnosed as an infection
- Uncommon for a bartolin gland abscess to occur in a postmenopausal woman
Adenocarcinoma

- Bartholin gland
- Paraurethral glands
- Apocrine glands

- High local recurrence rate
- Early LN spread
- Multimodality therapy required
- Deep dissection
Basal Cell Carcinoma

- 2-4% Vulvar cancers
- Local invasion
  - Rodent ulcer
- Rare LN spread
- Treat with radical local excision
Sarcomas

- Rare, 1-2% Vulvar cancers
- Multiple subtypes
- Often present as a large mass

- Wide local excision
- Multimodality therapy?
Verrucous Carcinoma

- Large, cauliflower like tumor
- Locally destructive
- Similar appearance to giant condyloma
- Low grade exophytic tumor
- Radical local excision, then repeat.
Pagets

- Elderly white caucasian women
- Itching, pain
- Well demarcated erythematous area with white islands (cake icing)
Pagets

- 17% have an underlying adenocarcinoma of the vulva
- 8-18% have a synchronous carcinoma
  - Breast, colorectal, bladder, Gyn
Paget’s

- Wide local excision
- Disease often extends beyond visible lesion
- Recurrence common with (70%) or without positive (38%) margins
- Imiquimod – off label

- Evaluate for other malignancy
Squamous Cell Carcinoma

- Itching
- Irritation
- Mass
- Ulceration
- 5% multifocal disease
- Examine entire lower genital tract and anus
- Symptoms present for over 12 months in 50% of patients
SCC - Risk Factors

- HPV Infection
- Immunosuppression
- Lichen Sclerosis
- VIN
- Smoking
- Age
SCC- Spread

- Direct extension
- Lymphatic
- Hematogenous
Lymphatic Spread

Diagram showing lymphatic spread from inguinal femoral nodes to iliac nodes via deep and superficial pathways.
SCC Staging FIGO 2009

- **STAGE I** Lesions confined to the vulva

- **STAGE II** Tumor of any size with extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus) with negative nodes

- **STAGE III** Tumor of any size with or without extension to adjacent perineal structures (lower 1/3 urethra, lower 1/3 vagina, anus) with positive inguino-femoral lymph nodes

- **STAGE IV** Tumor invades other regional (upper 2/3 urethra, upper 2/3 vagina), or distant structures
SCC Staging FIGO 2009

STAGE 0 Carcinoma in situ, intraepithelial neoplasia Grade III

STAGE I Lesions confined to the vulva
- Stage IA: Lesions ≤ 2 cm confined to the vulva or perineum and with stromal invasion ≤ 1.0 mm, no nodal metastasis
- Stage IB: Lesions > 2 cm confined to the vulva or perineum OR stromal invasion > 1.0 mm, no nodal metastasis

STAGE II Tumor of any size with extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus) with negative nodes

STAGE III Tumor of any size with or without extension to adjacent perineal structures (lower 1/3 urethra, lower 1/3 vagina, anus) with positive inguino-femoral lymph nodes
- STAGE IIIA(i) with 1 lymph node metastasis (≥5 mm)
- STAGE IIIA(ii) 1–2 lymph node metastases(es) (<5 mm) STAGE IIIB(i) with 2 or more lymph node metastases (≥5 mm)
- STAGE IIIB(ii) 3 or more lymph node metastases (<5 mm)
- STAGE IIIC with positive nodes with extracapsular spread

STAGE IV Tumor invades other regional (upper 2/3 urethra, upper 2/3 vagina), or distant structures
- Stage IVA(i): invades upper urethral and/or vaginal mucosa, bladder mucosa, rectal mucosa, or fixed to pelvic bone, or
- Stage IVA(ii): fixed or ulcerated inguino-femoral lymph nodes
- Stage IVB: Any distant metastasis including pelvic lymph nodes
# TNM Staging

## Table 1: Staging vulvar cancer (TNM and International Federation of Gynecology and Obstetrics, FIGO)

<table>
<thead>
<tr>
<th>Primary tumor (T)</th>
<th>FIGO stages</th>
<th>Definition</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td></td>
<td>Primary tumor cannot be assessed</td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td></td>
<td>No evidence of primary tumor</td>
<td></td>
</tr>
<tr>
<td>Tis</td>
<td></td>
<td>Carcinoma in situ</td>
<td></td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Lesions 2 cm or less in size, confined to the vulva or perineum and with stromal invasion 1.0 mm or less</td>
<td>WLE, no LNE</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Lesions more than 2 cm size or any size with stromal invasion more than 1.0 mm, confined to the vulva or perineum</td>
<td>WLE, LNE ipsilateral</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumor of any size with extension to adjacent perineal structures (lower/distal 1/3 urethra, lower/distal 1/3 vagina, anal involvement)</td>
<td>Modified radical vulvectomy (hemivulvectomy, anterior or posterior vulvectomy), LNE bilateral</td>
</tr>
<tr>
<td>T3</td>
<td>IVA</td>
<td>Tumor of any size with extension to any of the following; upper/proximal 2/3 urethra, upper/proximal 2/3 vagina, bladder mucosa, rectal mucosa or fixed to pelvic bone</td>
<td>Neoadjuvant chemotherapy and selected surgery, no LNE</td>
</tr>
</tbody>
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### Regional lymph nodes (N)

<table>
<thead>
<tr>
<th>NX</th>
<th>Regional lymph nodes cannot be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>One or two regional lymph nodes with the following features</td>
</tr>
<tr>
<td>N1a</td>
<td>One or two node metastases, each 5 mm or less</td>
</tr>
<tr>
<td>N1b</td>
<td>One lymph node metastasis 5 mm or greater</td>
</tr>
<tr>
<td>N2</td>
<td>Regional lymph node metastasis with the following features</td>
</tr>
<tr>
<td>N2a</td>
<td>Three or more lymph node metastases each less than 5 mm</td>
</tr>
<tr>
<td>N2b</td>
<td>Two or more lymph node metastases 5 mm or greater</td>
</tr>
<tr>
<td>N2c</td>
<td>Lymph node metastasis with extracapsular spread</td>
</tr>
<tr>
<td>N3</td>
<td>Fixed or ulcerated regional lymph node metastasis</td>
</tr>
</tbody>
</table>

### Distant metastasis (M)

<table>
<thead>
<tr>
<th>M0</th>
<th>No distant metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>Distant metastasis (including pelvic lymph node metastasis)</td>
</tr>
</tbody>
</table>

**Abbreviations:** WLE, wide local excision; LNE, lymphonodectomy; FIGO, International Federation of Gynecology and Obstetrics.
Vulvar Cancer
Vulvar Cancer
Vulvar Cancer
Surgery

- Manage vulva lesion and lymph node assessment independently
- Unilateral vs Bilateral nodal assessment
Surgical excision - Move to less extensive local resection

Radical Resection for >IA disease
  2cm surgical margin
  >8mm pathological margin linked to decreased recurrence risk

Dissection down to urogenital diaphragm

Partial vulvectomy
Radical vulvectomy

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Surgical Excision Closure

- Primary closure
- Left open - Granulation
- Full thickness flap - Rhomboid flap
- Myocutaneous graft - Gracilis
- Exenteration
Lymph Node Evaluation

- Prognostic
- Direct adjuvant therapy
- Therapeutic
- Unilateral vs Bilateral
Lymph node evaluation

- Sentinel node biopsy
  - Less lymphedema
  - Cost
  - Time
  - Long learning curve

- Lymph node dissection
  - More morbidity
  - Needed if no sentinel node identified
Sentinel LN Biopsy

- Peritumor injection of radioactive colloid and vital blue dye
- Excision of “active“ node only
Neo-Adjuvant Therapy

- Locally advanced/Unresectable disease
  - Radiation therapy with 5-FU or platinum chemotherapy
  - Follow with resection of residual tumor bed
  - Up to 50% have no residual tumor
  - Goal to reduce morbidity from extensive dissection, incontinence or colostomy formation etc
Radiation Therapy

- Un-resectable local disease, +/- chemotherapy
- Positive resection margins
- Positive inguinal lymph nodes
- Recurrent disease
Chemotherapy

- Reserved for metastatic disease
- Taxanes, Platinums, Topotecan, 5FU
- Palliative- Short prolongation of progression free survival
Recurrent Disease

- Vulvar— resection
- Groin recurrence – poor prognosis – Surgery + Radiation
- Distant recurrence – Chemotherapy- Palliative
A 72-year-old woman requests evaluation for chronic pruritis and soreness in the left labium majus. Self-application of talc and topical anti-fungal cream has not provided relief of her symptoms. Examination shows a 3-cm erythematous scaling patch on the inferior aspect of the left labium majus. The lesion is biopsied, and the histopathology is illustrated in the photograph.
Question 1

Which of the following is the most likely diagnosis?
- Dysplastic nevus
- Paget's disease
- Malignant melanoma
- Squamous cell carcinoma in situ (CIS)

Which of the following is the most appropriate treatment for this patient?
- Wide local excision
- Topical 5-fluorouracil
- Simple left hemi-vulvectomy
- Radical local excision with left inguinal-femoral lymphadenectomy
Question 1

Question 1: Which of the following is the most likely diagnosis?
Answer: B - Paget's disease

Question 2: Which of the following is the most appropriate treatment for this patient?
Answer: A - Wide local excision

Paget's disease of the vulva primarily affects caucasian women in the later post-menopausal years and accounts for less than 5% of vulvar neoplasms. Affected women usually present with pruritis. Physical examination usually shows a solitary lesion or multifocal patches of erythematous, weeping or scaly skin that resembles chronic eczema. The diagnosis is made by biopsy, and histology usually shows large, pale-staining adenocarcinoma (Paget) cells that are almost always confined to the epithelium. Local excision with a 2 cm peripheral margin is standard therapy for isolated Paget's disease, as Paget cells are often microscopically beyond the visible border of the lesion. If stromal invasion is found, then radical excision with lymph node dissection is warranted. Recurrence is common and may even occur in autologous skin grafts from distant donor sites. A concurrent secondary malignancy is found in up to 50% of cases of vulvar Paget's disease, most commonly adenocarcinoma of the breast or colon or
A 70-year-old woman with infrequent gynecologic care is referred from the Primary Care Clinic for evaluation of a painful mass on the vulva. The patient mentions that she has had a long history of vulvar pruritis for which she has intermittently used over-the-counter antifungal agents. She first noted a small lump on the vulva approximately six months ago, but the discomfort has increased over the last three months. On examination, there was a 2.1 cm exophytic, erythematous lesion involving the medial aspect of the left labium majus. The remainder of the pelvic examination, including visual inspection and palpation, was negative. A biopsy was performed, and the histopathology is depicted in the photomicrographs, which demonstrate low-power (Figure 1) and high-power (Figure 2) images of the lesion.
Question 2

Which of the following is the most likely diagnosis?
- VIN 3
- Squamous hyperplasia with atypia
- Invasive squamous cell carcinoma
- Melanoma

Which of the following is the most appropriate treatment for this patient?
- Simple vulvectomy
- Radical vulvectomy with ipsilateral inguinal lymph node assessment
- Radical vulvectomy with bilateral inguinal lymph node assessment
- Radiation therapy
Question 2

Question 1: Which of the following is the most likely diagnosis?
Answer: C - Invasive squamous cell carcinoma

Question 2: Which of the following is the most appropriate treatment for this patient?
Answer: B - Radical vulvectomy with ipsilateral inguinal lymph node assessment

Squamous cell carcinoma is the most common type of vulvar carcinoma, typically occurring in the seventh and eighth decades of life. A long history of vulvar pruritis is a common finding. Spread of the tumor follows lymphatics, first involving the superficial inguinal nodes, followed by the deep femoral nodes, then the pelvic nodes. Nodal involvement depends on tumor size and stage; even with small lesions (<2 cm), groin nodes are positive in approximately 20% of cases. If groin nodes are positive, pelvic nodes will be positive in approximately 25% of patients. Treatment usually is radical vulvectomy with ipsilateral groin dissection. Primary radiation has been studied. However, due to difficulty in directing external beam therapy to the area, and the complications that may arise due to the poor tolerability of the vulvar epithelium and mucosa near the vestibule, primary radiation therapy rarely is used.
An 83-year-old woman requested evaluation because of vulvar pain. Physical examination showed a left vulvar lesion (Figure 1) and an enlarged left inguinal node. Biopsy of the vulvar lesion is shown in Figure 2.

Which of the following is the most likely diagnosis?
- Melanoma
- Adenocarcinoma
- Squamous cell carcinoma
- Sarcoma
Which of the following factors is most predictive of the patient's probability of survival?

- Lesion size
- Differentiation
- Nodal spread
- Tumor ploidy

Which of the following is the most appropriate treatment for this patient?

- Wide local excision
- Modified radical vulvectomy
- Modified radical vulvectomy and unilateral groin dissection
- Modified radical vulvectomy and bilateral groin dissection
Question 3

Question 1: Which is the most likely diagnosis?
Answer: C - Squamous cell carcinoma

Question 2: Which is most predictive of the patient's probability of survival?
Answer: C - Nodal spread

Question 3: Which is the most appropriate treatment for this patient?
Answer: D - Modified radical vulvectomy and bilateral groin dissection

Squamous cell carcinomas comprise 90% of vulvar cancers. Melanoma is second in frequency, occurring in 5% of cases. Groin node status is the most important factor influencing survival. With negative nodes, the five-year survival is 90%, versus 50-60% in those with positive nodes. Modified radical vulvectomy is usually sufficient to remove the primary lesion. A unilateral groin dissection can only be performed in patients with a well-lateralized, small (<2 cm) lesion without ipsilateral nodal spread. In view of the present patient's lymphadenopathy, she should have a bilateral lymph node dissection.
A 40-year-old homeless female was transported to the emergency room after being found unresponsive on a park bench. You are called to evaluate the patient's large vulvar mass (see illustration). When the patient is clinically stable and alert, you perform a biopsy of the mass. The preliminary pathology report is consistent with a sarcoma.
Question 4

- Which of the following is the most common histologic type of vulvar sarcoma?
  - Liposarcoma
  - Angiosarcoma
  - Epithelioid sarcoma
  - Leiomyosarcoma

- Which of the following is the usual treatment for a vulvar sarcoma?
  - Radiation
  - Wide surgical excision
  - Chemotherapy
  - Immunotherapy
Question 1: Which of the following is the most common histologic type of vulvar sarcoma?
Answer: d. Leiomyosarcoma

Question 2: Which of the following is the usual treatment for a vulvar sarcoma?
Answer: b. Wide surgical excision

Sarcomas represent approximately 1 to 2% of vulvar malignancies, and the most common histologic type is leiomyosarcoma. The primary treatment is wide surgical excision; however, with high grade tumors, adjuvant radiation may be considered. Recurrence of the tumor appears to be associated with large lesions >5 cm in diameter, lesions with infiltrating margins, and lesions with 5 or more mitotic figures per high powered field.
Questions?