ARROCase: Vaginal Cancer

Anna Lee, MD, MPH (PGY-1)
Lauren Tait, MD (PGY-5)
Faculty: Jyoti Mayadev, MD
University of California Davis Comprehensive Cancer Center
Department of Radiation Oncology
May 13, 2015
Overview

• Case Presentation
• Background
• Risk Factors
• Clinical Manifestations
• Workup
• Staging
• Management
• Surveillance and Follow up
Case Presentation

• **CC:** Vaginal discharge and spotting

• **HPI:** 82yo CF *s/p hysterectomy 50 years ago for benign disease* who c/o 6-month hx of vaginal discharge and spotting.
  
  – Gyn Onc’s pelvic exam revealed extensive *tumor* involving the anterior and posterior wall of the vagina extending nearly to the introitus, sparing the urethral meatus. Rectovaginal exam confirmed *paravaginal extension with thickening of the vaginal apex,* suspicious for pelvic extension.
  
  – CT revealed surgically absent cervix and uterus with *vaginal wall thickening,* no LAD.
• PELVIC EXAM FINDINGS
  – Visual exam
    • Normal atrophic external female genitalia
  – Bimanual exam
    • firm circumferential mass beginning 1.5cm proximal to introitus extending entire length of the vagina without frank involvement of the urethral meatus
  – Speculum exam
    • poorly tolerated but confirmed BME
  – Rectovaginal exam
    • confirmed mild paravaginal extension bilaterally
PET-CT Scan
Maximum Intensity Projection (MIP): PA coronal view

-> more prominent on the left
Diagnosis

• Vaginal biopsy results
  – Squamous cell carcinoma
  – High grade
  – Less differentiated
  – Keratinization

• FIGO Stage II (T2N0MO)

# Staging

**AJCC 7th Ed., 2010/FIGO 2008**

<table>
<thead>
<tr>
<th>TNM CATEGORIES</th>
<th>FIGO STAGES</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumor (T)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TX</td>
<td></td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>I</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>II</td>
<td>Tumor confined to vagina</td>
</tr>
<tr>
<td>T2</td>
<td>III</td>
<td>Tumor invades paravaginal tissues but not to pelvic wall*</td>
</tr>
<tr>
<td>T3</td>
<td>IVA</td>
<td>Tumor extends to pelvic wall*</td>
</tr>
<tr>
<td>T4</td>
<td></td>
<td>Tumor invades mucosa of the bladder or rectum and/or extends beyond the true pelvis (bullous edema is not sufficient evidence to classify a tumor as T4)</td>
</tr>
</tbody>
</table>

| Regional lymph nodes (N) |             |            |
| NX             |             | Regional lymph nodes cannot be assessed |
| N0             |             | No regional lymph node metastasis |
| N1             | III         | Pelvic or inguinal lymph node metastasis |

| Distant metastasis (M) |             |            |
| M0             |             | No distant metastasis |
| M1             | IVA         | Distant metastasis |

## ANATOMIC STAGE/PROGNOSTIC GROUPS

| Stage I | T1 | N0 | M0 |
| Stage II| T2 | N0 | M0 |
| Stage III| T1-T3 | N1 | M0 |
|          | T3 | N0 | M0 |
| Stage IVA| T4 | Any N | M0 |
| Stage IVB| Any T | Any N | M1 |

*Pelvic wall is defined as muscle, fascia, neurovascular structures, or skeletal portions of the bony pelvis. On rectal examination, there is no cancer-free space between the tumor and pelvic wall.*
Case Definitive Tx Plan

• IMRT at outside hospital + Concurrent Chemotherapy (cisplatin) ➔ Interstitial Brachytherapy
  – IMRT with 45 Gy to the whole pelvis and inguinal nodes in 25 total fractions over 5 weeks
  – Interstitial vaginal high dose rate brachytherapy with 24 Gy in 4 total fractions with 2 planned insertions over 2 weeks
IMRT Planning

Outside Hospital

ASSOCIATION OF RESIDENTS IN RADIATION ONCOLOGY
HDR #1 DVH
HDR Brachy Planning #2
# Dosimetric Values

### Interstitial #1
- ICRU Bladder point: 390 cGy
- ICRU Rectal point: 387 cGy
- D2cc Rectum: 310 cGy
- D2cc Bladder: 380 cGy
- D2cc Sigmoid: 180 cGy
- D2cc Bowel: 370 cGy

### Interstitial #2
- ICRU Bladder point: 367 cGy
- ICRU Rectal point: 581 cGy
- D2cc Rectum: 480 cGy
- D2cc Bladder: 460 cGy
- D2cc Sigmoid: 430 cGy
Case Summary

• 82 WF with FIGO stage II (T2N0M0) vaginal cancer of squamous cell histology that was high grade, keratinized

• Treatment course
  – IMRT with 45 Gy to the whole pelvis and inguinal nodes in 25 total fractions over 5 weeks with concurrent cisplatin
  – Followed by interstitial vaginal high dose brachytherapy with 24 Gy in 4 total fractions with 2 planned insertions over 2 weeks.

• 1.5 years later, she remains without evidence of disease

• Treatment side effects
  – Mild vaginal foreshortening, no vaginal mucosal changes, no ulcerations
Background

• Primary vaginal cancer accounts for 3% of all malignant neoplasms of the female genital tract
  – Most are of squamous cell histology
  – Most are detected in women ≥ 60 yo
• Majority (75%) of vaginal malignancies are metastatic, which occur by direct extension or by lymphatic or hematogenous spread
Risk Factors

• Most are mediated by HPV infection
• Same risk factors as cervical cancer
  – Number of lifetime sexual partners
  – Early age at first intercourse
  – Current smoker
• Many have a prior history of gynecologic malignancy
Clinical Manifestations

- Vaginal bleeding (most common)
- Discharge
- Pruritus
- Dyspareunia
- Pelvic pain
- Change in bowel/bladder habits
- Many are asymptomatic
Anatomy

- Upper two thirds of the vagina drains to the obturator, internal, external and common iliac nodes
- Lower one third of the vagina drain to the inguinofemoral nodes
- Vaginal cancer is most often found in the posterior wall, superior one third of the vagina
Workup for FIGO Staging

• Physical exam of pelvis and vagina
  – Speculum examination (rotate to observe posterior wall), vaginal palpation, bimanual pelvic, rectovaginal for staging
• Biopsy of suspicious lesions on vagina, vulva, cervical os, inguinal/femoral nodes
• Cystoscopy and/or proctosigmoidoscopy for locally advanced disease
• CXR, CBC, LFTs and ALP
Additional Workup for Management

• Advanced imaging does not contribute to FIGO staging
  – CT, MRI, PET/CT to assess extent of disease and treatment planning
• **Note:** cancer involving the vulva or cervix is not considered to be a vaginal primary
Overall DFS and Prognosis

- The most significant prognostic factor is anatomic staging, which reflects the extent of invasion into the surrounding tissue or of metastatic spread.
- Other factors include >60 years of age, symptomatic at diagnoses, lesions of middle and lower 1/3 of vagina, poorly differentiated tumors, length of vaginal wall involvement.

Screening

• While unproven, PAP smears of the vaginal vault in elderly women who have had hysterectomy for (pre)invasive cervical cancer is reasonable

• Insufficient evidence to recommend routine vaginal smear screening in women after total hysterectomy for benign disease
Standard Tx Options

**Biopsy** to confirm diagnosis of invasive disease

**Assess extent of disease**
- Evaluate for synchronous in-situ or invasive disease (cervix, vulva, anus)
- EUA for locally advanced or bulky disease
- Consider cystoscopy and proctoscopy

**Imaging studies as available**
- PET/CT to evaluate for nodal and distant metastasis
- MRI to define local disease extent and assist in planning brachytherapy

**Small-volume primary disease** (stage I)
- No node metastases or extension to functionally important organs (bladder, rectum, urethra)
  - or
- **Stage IVA bulky disease with fistula**
  - Rectovaginal, vesicovaginal

**Consider primary surgery**
- Stage I: partial vaginectomy ± hysterectomy ± lymphadenectomy
- Stage IVA with fistula: total vaginectomy; selective exenteration ± lymphadenectomy

**Primary irradiation**
- Inadequate margins.
- Node metastasis

**Extensive disease** (unsuitable for conservative surgery alone)
- Primary tumor encroaches on functional midline structures (urethra, bladder, rectum)
- Evidence of regional node spread
- Vaginal involvement that precludes surgical preservation of sexual function

**Consider synchronous chemotherapy**
- Initial teletherapy to encompass primary tumor, regional extensions, first echelon lymph nodes
- Reduced volume boost (brachytherapy or teletherapy) to site(s) of initial macroscopic metastases
- Surgical salvage for persistent or recurrent cancer

---

*Wide excisional biopsy: appropriate in small stage I lesions if not functionally deforming.*
†Value of synchronous chemoradiation unproven for vaginal cancer at this time.
‡Margins =5 mm (arbitrary).

Definitive RT for Stage I

- **<0.5cm**: EBRT or IC ± IS, tx entire vaginal mucosa to 65 Gy with additional mucosal dose of 20-30 Gy to area of tumor involvement
  - Evidence
    - Overall, local control rates with brachytherapy alone range from 67-100%
    - 18% local failure rate with brachytherapy alone (Dancuart et al., 1988)

- **>0.5cm**: EBRT to whole pelvis ± inguinal LN to 45 Gy, followed by IS ± IC boost to tumor with 2cm radial margin to 70-80 Gy
  - Evidence
    - Tumor control the same with brachytherapy alone vs. EBRT followed by brachy (Perez et al., 1988)
Definitive RT for Stage II

• EBRT to whole pelvis ± inguinal LN to 45 Gy, followed by IS ± IC boost to tumor with 2cm radial margin to 70-80 Gy
  – Evidence
    • 36% pelvic tumor CR with brachytherapy alone vs. 67% CR with combined EBRT and brachytherapy (Perez et al., 1988)
    • 5-year PDC rate 84% and DSS rate 78% for Stage II receiving definitive RT (Frank et al., 2005)
Definitive RT for Stages III, IVA

- EBRT to whole pelvis + pelvic/inguinal LN to 45 Gy, followed by IS ± IC boost to tumor of 75-85 Gy and dose to lateral pelvic wall of 55 Gy to 60 Gy
  - Evidence
    - Only 20-30% of patients achieve local control. Pelvic recurrence occur more often than distant recurrences (Frank et al., 2005)
Chemoradiation

• No randomized trials
• Concurrent 5-FU and/or cisplatin chemotherapy with irradiation for advanced carcinoma (III, IVA, tumors larger than 4cm)
  – Evidence:
    • Cisplatin-based CRT 44% disease free over a mean follow-up time of 129 months (Frank et al., 2005)
    • 12 patients Stage II-IVA received CRT with Cisplatin, EBRT, brachytherapy; overall well tolerated; 5-year OS 66%, PFS 75%, locoregional PFS 92% (Samant et al., 2007)
    • 14 patients Stage I-III, non-surgical candidates, received CRT w 5-FU alone, w cisplatin or mitomycin-C; cancer control outcomes more favorable than prev studies with high dose RT alone (Dalrymple et al., 2004)
Considerations for the Post-Hysterectomy Patient

• 60% have had a previous hysterectomy

• Anatomical changes s/p hysterectomy
  – Small bowel tends to fall lower into the pelvis, increasing the likelihood of it being irradiated during treatment
  – Vaginal vault position varies more

• Technique to minimize under-dosing the target:
  – Fuse planning CT scans taken with full and empty bladder to estimate potential range of target volume positions
  – Fill the bladder with a fixed volume of saline using a Foley catheter immediately prior to treatment
Surveillance & Follow-up

- No reliable evidence that routine cytologic or imaging improves outcomes beyond PE and assessment of new symptoms
- Given the pt’s locally advanced disease and tx regimen, consider pelvic exam and pap smear
  - q3months for year 1
  - q4months for year 2
  - q6months for years 3-5
  - then annually
- CXR annually for 5 years
- PET-CT if recurrence suspected

Salani et al., 2011
# RT-Related Toxicities

## Whole Pelvis EBRT
- **Early**
  - Diarrhea, bladder irritation (urgency, frequency, dysuria, hematuria, fatigue)
- **Late**
  - GI: change in bowel habits, rectal bleeding, stricture, ulcer, fistula
  - GU: chronic cystitis, urinary sx
  - Vaginal: stenosis, dryness, fibrosis, fistula
  - Fertility: ovarian dysfxn, menopause, poor uterine expansion
  - MSK: lumbosacral neuropathy and/or pelvic insufficiency fx

## Interstitial Brachytherapy
- Vaginal stenosis, necrosis, rectovaginal and/or vesicular vaginal fistula formation, rectal injury, bladder, injury, vaginal bleeding, discharge, infection, hemorrhagic cystitis
References


• Please provide feedback regarding this case or other ARROcases to arrocase@gmail.com