Urine Papillary Serous Carcinoma

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Introduction

- Serous Endometrial Carcinoma represents approximately 10% of endometrial carcinomas.
- The tumors often deeply invade the myometrium.
- It has the tendency for peritoneal spread, unlike typical endometrial adenocarcinoma.

Introduction

- Advanced Disease presentation is common
- Recurrence of the disease is very high
- Even in cases of minimally invasive or confined to the endometrium in polyps
- Spread rate to adenexia is 50%

Introduction

- 60% of cases will be upstaged after complete surgical staging (Microscopic identification)
- Closely resembles serous carcinoma of Ovary and Fallopian tube
- Lymphatic invasion is commonplace in myometrium
- Psammoma bodies frequently observed

The Proportional Hazards of relative survival time (Clinical Stage I and II)


- **Serous Carcinoma**
  - Grade 1 RR 2.9
  - Grade 2 RR 4.4
  - Grade 3 RR 6.6

- **Endometrioid Ca**
  - Grade 1 RR 1
  - Grade 2 RR 1.6
  - Grade 3 RR 2.6
**Diagnosis**

- Typically Diagnosed on endometrial biopsy prompted by postmenopausal bleeding
- It is not hormone sensitive, so it does not develop from endometrial hyperplasia
- It arises in setting of endometrial atrophy

The median age at diagnosis of 138 women in the Goldberg et al study was 67 years.

- 54 (40%) women diagnosed at stage I
- 20 (14%) women at stage II
- 41 (30%) women at stage III
- 23 (16%) women at stage IV

Goldberg et al. Gynecol Oncol. 2008 Feb;108(2):298-305
Management

- Regular Metastatic workup
- Surgical staging (+Cytology) with Total abdominal Hysterectomy, Bilateral Salpengoophrectomy, Omentectomy and Lymphadenectomy
- Adjuvant Chemotherapy and Radiotherapy
Uterine Neoplasms

Kingdom of Saudi Arabia
National Guard Health Affairs
King Abdulaziz Medical City – Jeddah
King Khaled Hospital
Princess Norah Oncology Center (PNOC)

PNOC PRACTICE GUIDELINES IN ONCOLOGY
Table 1
International Federation of Gynecology and Obstetrics (FIGO) and Tumor-Node-Metastases (TNM) Surgical Staging Systems for Endometrial Cancer*

<table>
<thead>
<tr>
<th>FIGO Stages</th>
<th>Surgical-Pathologic Findings</th>
<th>TNM Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Carcinoma in situ (preinvasive carcinoma)</td>
<td>Tis</td>
</tr>
<tr>
<td>I</td>
<td>Tumor confined to the corpus uteri</td>
<td>T1</td>
</tr>
<tr>
<td>IA</td>
<td>Tumor limited to endometrium</td>
<td>T1a</td>
</tr>
<tr>
<td>IB</td>
<td>Tumor invades one half or less of the myometrium</td>
<td>T1b</td>
</tr>
<tr>
<td>IC</td>
<td>Tumor invades more than one half of the myometrium</td>
<td>T1c</td>
</tr>
<tr>
<td>II</td>
<td>Tumor invades cervix but does not extend beyond uterus</td>
<td>T2</td>
</tr>
<tr>
<td>IIA</td>
<td>Endocervical glandular involvement only</td>
<td>T2a</td>
</tr>
<tr>
<td>IIB</td>
<td>Cervical stromal invasion</td>
<td>T2b</td>
</tr>
<tr>
<td>III</td>
<td>Local and/or regional spread as specified in IIA, B, C and/or N1</td>
<td>T3</td>
</tr>
<tr>
<td>IIIA</td>
<td>Tumor involves serosa and/or adnexa (direct extension or metastasis) and/or cancer cells in ascites or peritoneal washings</td>
<td>T3a</td>
</tr>
<tr>
<td>IIIB</td>
<td>Vaginal involvement (direct extension or metastasis)</td>
<td>T3b</td>
</tr>
<tr>
<td>IIIC</td>
<td>Metastasis to pelvic and/or para-aortic lymph nodes</td>
<td>N1</td>
</tr>
<tr>
<td>IVA</td>
<td>Tumor invades bladder mucosa and/or bowel mucosa (the presence of bullous edema is not sufficient to classify tumor as T4)</td>
<td>T4</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastasis (excluding metastasis to vagina, pelvic serosa, or adnexa; including metastasis to intra-abdominal lymph nodes other than para-aortic and/or inguinal lymph nodes)</td>
<td>M1</td>
</tr>
</tbody>
</table>


†All cases of FIGO stage I-IVA should be subclassified by histologic grade as follows: GX = grade cannot be assessed; G1 = well differentiated; G2 = moderately differentiated; G3 = poorly differentiated or undifferentiated.
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Uterine Neoplasms - 2009

UTERINE NEOPLASMS INITIAL WORKUP AND CLASSIFICATION

INITIAL EVALUATION

- H&P
- CBC, platelets
- Endometrial biopsy
- Chest x-ray
- Current cervical cytology
- LFT/renal function tests/chemistry profile

Pathology Review

INITIAL CLINICAL FINDINGS

Pure Endometrioid

- Disease limited to uterus
- Suspected or gross cervical involvement
- Suspected extrauterine disease

Epithelial carcinoma

- Papillary serous or clear cell carcinoma

Carcinosarcoma

Stromal/mesenchymal tumors
- Endometrial stromal sarcoma (ESS)
- High-grade undifferentiated sarcoma (HGUD)
- Leiomyosarcoma (LMS)

Disease limited uterus

Known or suspected extrauterine disease

See Primary Treatment Of Endometrial Carcinoma

See Primary Treatment Of Endometrial Carcinoma

See Primary Treatment Of Endometrial Carcinoma

See Treatment for Papillary Serous or Clear Cell Carcinomas of the Endometrium or Carcinosarcoma

See Primary Treatment Of Endometrial Carcinoma

See Primary Treatment Of Endometrial Carcinoma

See Primary Treatment Of Endometrial Carcinoma

Staged aggressively, should be treated as a high grade endometrial cancer.

Also known as malignant mixed mesodermal tumor or malignant mixed Müllerian tumor and including those with either homologous or heterologous stromal elements.

By definition, ESS is a low-grade sarcoma.
Endometrial Carcinoma
Uterine Limited Disease

INITIAL CLINICAL FINDINGS

- Medically inoperable
  - Radical RT
  - See Surveillance

- Disease limited to the uterus (endometrioid histologies)
  - Operable
    - Total hysterectomy and bilateral salpingo-oophorectomy (TH/BSO)
      - Cytology
      - Lymph node dissection (Not random sampling) In cases of: G3, pap – serous and clear cell histologies:
        - Pelvic lymphadenectomy
        - Para-aortic lymphadenectomy
    - See Adjuvant treatment for incompletely surgically staged

- Adjuvant Treatment for completely surgically staged:
  - Stage I
  - Stage II
  - Stage IIIA
  - Stage IIIB-IV

a See (page - 3) for clarification of uterine neoplasms.
b See Hysterectomy
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Uterine Neoplasms - 2009

Endometrial Carcinoma
Suspected or gross cervical involvement

INITIAL CLINICAL FINDINGS

Suspected or gross cervical involvement (endometrioid histologies)\(^a\)
Consider cervical biopsy or MRI

ADDITIONAL WORKUP

Negative result

Operable

Positive result or Gross involvement

PRIMARY TREATMENT

TH/BSO\(^b\)
- Cytology
- Lymph node dissection (not random sampling)
  - Pelvic lymphadenectomy
  - Para-aortic lymphadenectomy

Incompletely surgically staged
See Adjuvant treatment for incompletely surgically staged

Operable

Radical hysterectomy and bilateral salpingo-oophorectomy (RH/BSO)\(^c\)
- Cytology
- Lymph node dissection (not random sampling)
  - Pelvic lymphadenectomy
  - Para-aortic lymphadenectomy

Adjuvant Treatment for completely surgically staged:
- Stage I
- Stage II
- Stage IIIA
- Stage IIIB-IV

Operable

Inoperable
Radical XRT

See Surveillance

See (page - 3) for clarification of uterine neoplasms.

See Hysterectomy

PNOC Practice Guidelines In Oncology – Version 2009
Endometrial Carcinoma
Suspected extrauterine disease

INITIAL CLINICAL FINDINGS

Suspected extrauterine disease (endometrioid histologies)\(^a\)

- CA-125
- MRI/CT, as clinically indicated

ADDITIONAL WORKUP

- Intra-abdominal:
  - Ascites
  - Omentum
  - Nodal
  - Ovarian
  - Peritoneal

- Extrauterine pelvis:
  - Vaginal
  - Bladder
  - Bowel/rectum
  - Parametrial

- Extra-abdominal/ liver

PRIMARY TREATMENT

- See Primary Treatment (disease limited to uterus)
- TH/BSO + cytology + maximal debulking ± pelvic and para-aortic lymph node dissection + Omentectomy
- Adjuvant treatment for completely surgically staged:
  - Stage IIIA
  - Stage IIIB-IV
- Chemotherapy ± XRT
- See Surveillance
- Chemotherapy Consider palliative TH/BSO ± RT

\(^a\) See (page - 3) for clarification of uterine neoplasms.
\(^b\) See Hysterectomy
Endometrial Carcinoma
Adjuvant treatment for completely surgically staged: Stage I

<table>
<thead>
<tr>
<th>CLINICAL FINDINGS</th>
<th>ADVERSE RISK FACTORS</th>
<th>HISTOLOGIC GRADE/ADJUVANT TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>G1</td>
</tr>
<tr>
<td>Stage IA</td>
<td>Adverse risk factors not present</td>
<td>Observe</td>
</tr>
<tr>
<td></td>
<td>Adverse risk factors present</td>
<td>Observe</td>
</tr>
<tr>
<td>Stage IB (≤ 50%)</td>
<td>Adverse risk factors not present</td>
<td>Observe</td>
</tr>
<tr>
<td></td>
<td>Adverse risk factors present</td>
<td>Observe</td>
</tr>
<tr>
<td>Stage IC</td>
<td>Adverse risk factors not present</td>
<td>Vaginal brachytherapy</td>
</tr>
<tr>
<td></td>
<td>Adverse risk factors present</td>
<td>vaginal brachytherapy</td>
</tr>
</tbody>
</table>

1. Potential adverse risk factors include the following: > 60 y, positive lymphovascular invasion, tumor size, lower uterine involvement

2. Adjuvant therapy determinations are made on the basis of pathologic findings.

3. Adjuvant pelvic RT: 45-50 Gy to clinical tumor volume (CTV).

4. The role of adjuvant chemotherapy in invasive high grade uterine confined disease is the subject of current studies.
Endometrial Carcinoma

Adjuvant treatment for completely surgically staged: Stage II

**Clinical Findings**

<table>
<thead>
<tr>
<th>Myometrial invasion</th>
<th>Stage IIA</th>
<th>Stage IIB³</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 50%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Histologic Grade/Adjuvant Treatment**¹²³

<table>
<thead>
<tr>
<th>GI</th>
<th>G2</th>
<th>G3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observe</td>
<td>Observe or Vaginal brachytherapy</td>
<td>Vaginal brachytherapy ± pelvic RT</td>
</tr>
<tr>
<td>Vaginal brachytherapy ± pelvic RT</td>
<td>Vaginal brachytherapy ± pelvic RT</td>
<td>Pelvic RT + vaginal brachytherapy</td>
</tr>
<tr>
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¹ Adjuvant therapy determinations are made on the basis of pathologic findings.
² Adjuvant pelvic RT: 45-50 Gy to clinical tumor volume (CTV).
³ The role of adjuvant chemotherapy in invasive high grade uterine confined disease is the subject of current studies.
⁴ Observation or vaginal brachytherapy is an option for patients with Stage IIB disease who are post primary radical hysterectomy, with negative surgical margins and no evidence of extraterine disease.
Endometrial Carcinoma

PAPILLARY SEROUS OR CLEAR CELL CARCINOMA OF THE ENDOMETRIUM OR CARCINOSARCOMA

PRIMARY TREATMENT

- Biopsy: papillary serous or clear cell carcinoma or Carcinosarcoma
- Includes surgical staging, as with ovarian cancer
- TH/BSO, pelvic and para-aortic lymph node dissection, cytology, omentectomy, biopsies of peritoneal surfaces (including underside of diaphragm)
- Maximal tumor debulking

ADJUVANT TREATMENT

- Stage IA (confined to polyp)
  - Observe or vaginal brachytherapy
- Other Stage IA disease (Not confined to polyp)
  - Chemotherapy + tumor directed RT
- Stage IB, IC, II
- Stage III, IV (adequately debulked)
- Stage III, IV (inadequately debulked)
  - Chemotherapy

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1 Also known as malignant mixed mesodermal tumor or malignant mixed Mullerian tumor and including those with either homologous or heterologous stromal elements
Management

- Goldberg et al. 138 women with UPSC followed up 1986 - 2003
- Median follow up for the surviving patients was 44 months
- 129 patients had surgery and 122 patients rendered free of gross disease and comprised the adjuvant group

Management

- 23 patients received platinum-based chemotherapy
- 52 patients had radiotherapy
- 28 Patients had combined chemo-radiotherapy

Management

- At last follow up:
  - 57 patients were alive free of disease
  - 10 patients alive with disease
  - 62 patients died of disease
  - 8 patients died of another causes
  - One patient died due to toxicity

Management

- Five year disease free survival (DFS) was 42%
- Disease specific survival (DSS) was 56%
- Overall Survival for the 122 patients treated with curative intent was 54%

Management

- Surgical treatment as the sole therapy for patient with UPSC is unacceptable
- Chemotherapy, radiotherapy or both have been added after surgery to improve survival
- Survival benefit to patients from such multimodality therapy remains uncertain

Management

- Pattern of failure after multimodality treatment studied by Sood et al
- 42 patients reviewed retrospectively between 1988 and 1998
- Median follow up for all patients was 19 months

Management

- 29 (69%) patients had recurrence at the time of last follow up
- Failure rate at 2 years was 58% and at 5 years was 67%
- 19 of 29 patients had recurrence in abdomen, vagina or pelvis (66%)

Management

- Metastases outside the abdomen 17% only
- 25 patients (60%) died at time of reporting
- 2 years survival rate is 52% and 5 years survival rate is 43%

Management

- No increased survival in stage I UPSC who had surgery and adjuvant radiation therapy versus observation
- Postsurgical chemotherapy in stage I may be beneficial but more data needed

Management

- 60% of UPSC cases were found to overexpress the protein HER2/neu
- Same protein overexpressed in some cases of breast cancer
- Monoclonal antibody Trastuzumab (Herceptin) has been tried with some success in phase II trial in UPSC with HER2/neu
