Endometrial Carcinoma

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Endometrial carcinoma

- Most common gynecologic malignancy in developed countries.

- Second most common in developing countries (cervical cancer is more common).

- **Endometrioid carcinoma**
- **Most common histologic type of endometrial carcinoma.**
- **Favorable prognosis**
- **Typically present at an early stage with abnormal uterine bleeding.**
- **Serous, Clear cell as well as other types of uterine cancer are associated with poor prognosis.**

EPIDEMIOLOGY

- Endometrial cancer develops in 1 to 2 percent of women
- fourth most common cancer in women.

- incidence:
- peaks between ages 60 and 70 years
- 2 to 5 percent before age 40 years.
- Women under age 50 who develop endometrial cancer are often at risk because of chronic anovulation and/or obesity.

HISTOPATHOLOGY

- **Type I** tumors:
- endometrioid histology grade 1 or 2
- approximately 80 percent of endometrial carcinomas.
- favorable prognosis,
- estrogen induced
- responsive to progestins,
- may be preceded by an intraepithelial neoplasm (atypical and/or complex endometrial hyperplasia)

- **Type II** tumors:
- 10 to 20 percent of endometrial carcinomas.
- Grade 3 endometrioid and tumors of nonendometrioid histology:
- Serous, clear cell, mucinous, squamous, transitional cell, mesonephric, and undifferentiated.

- Type 2 endometrial carcinomas tend to present at an advanced stage.

- Approximately 70 percent of patients with uterine serous cancer (USC) and 50 percent with clear cell cancers present with stage III or IV disease

Type 2 endometrial carcinomas have traditionally been thought to differ from type 1 tumors in several ways.

Some of these are well established, but others are controversial

- The average age at diagnosis is older for type 2 disease in most studies.
- prospective study of over one million Norwegian women follow up for an average of 25 years:
  - 992 type 2 carcinomas
  - Revealed no difference in age at diagnosis of type 1 and type 2 cancers (mean age, 65 years both groups) .
- By comparison, the average age at diagnosis of all uterine cancer in the United States is 62 years old

- Obesity
- risk factor for type 1 endometrial carcinomas not associated with type 2.
- Obesity is a risk factor for all endometrial carcinomas .
- in the Norwegian cohort study obesity was associated with an increased risk of either type of tumor, more pronounced for type 1

Type II Tumors

- more likely to be in parous than nulliparous
- different racial distribution than type 1 carcinomas.
- more likely in black women than White women with poorer overall prognosis

- uncertain relationship between breast cancer and USC
- personal history of breast cancer is associated with a risk of developing USC .

- women with **serous histology** were more likely than those with endometrioid histology to have a personal history of **breast cancer** (19 versus 3 percent) .

- This risk does not appear to be dependent upon use of tamoxifen.
- In addition, there have been some reports that the ***BRCA1* mutation** carriers are at an increased risk of USC

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Ten-Year Comparison Study of Type 1 and 2 Endometrial Cancers: Risk Factors and Outcomes

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- Type 2 tumors were more likely to be diagnosed at an older age (65.6 vs. 62.2, $p < 0.001$)
- lower BMI (32.2 vs. 34.3, $p = 0.03$),
- non-white race (23 vs. 12.7%, $p < 0.001$),
- postmenopausal (89.7 vs. 83.6%, $p = 0.02$),
- history of other malignancy (13.5 vs. 8.6%, $p = 0.03$).
- statistically higher gravidity (2.56 vs. 2.15, $p = 0.005$) and parity (2.13 vs. 1.77, $p = 0.004$).
- Both types had similar rates of smoking, diabetes, hypertension, use of hormone replacement therapy (HRT), and use of oral contraceptive pills.

- Type 2 cancer is diagnosed with a higher nuclear grade ($p < 0.001$),
- more likely to have lymphovascular space invasion (43.1 vs. 17.8%, $p < 0.001$),
- lower uterine segment involvement (55.2 vs. 42.4%, $p = 0.001$),
- higher depth of myometrial invasion (41.6 vs. 28.8%, $p < 0.001$),
- higher stage ($p < 0.001$).

- Type 2 disease has the highest association with both:
- recurrence (HR 3.44, 95% CI 1.75– 6.77, $p < 0.001$)
- death (HR 2.99, 95% CI 1.87–4.77, $p < 0.001$)
- In addition to cancer type (2) and stage(3-4) myometrial invasion was associated with increased risk of recurrence and death

Serous endometrial carcinoma

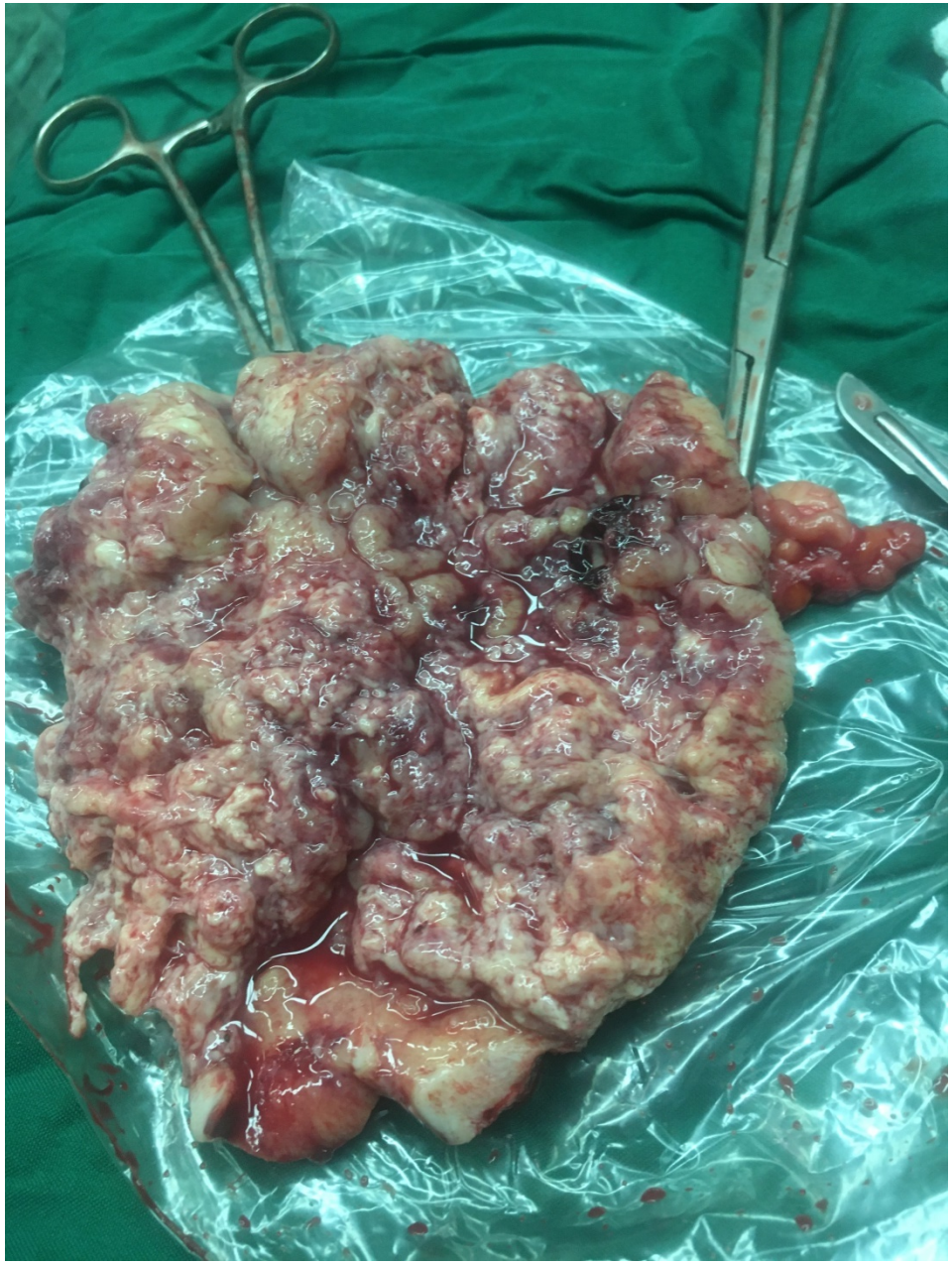
- the second most common type of EC but only accounts for approximately 10 percent of cases.

- A very large majority of SECs are of the p53abn molecular subtype.
- *HER2* is overexpressed/amplified/mutated in a minority of SECs and can be targeted therapeutically.

- Clinically occult extrauterine disease is often present at diagnosis .

- SEC often diffusely infiltrates the myometrium and may have extensive lymphovascular space invasion and peritoneal spread, similar to ovarian carcinoma.

- However, SEC confined to the endometrium (or a polyp) with minimal myometrial invasion and no distant disease after surgical staging has a good prognosis.



Clear cell carcinoma

- an uncommon subtype, comprising <5 percent of EC, and patients are usually older, postmenopausal patients .

- Clear cell ECs four molecular subtypes;
- *POLE*mut clear cell carcinomas have the most favorable prognosis while p53abn clear cell carcinomas are associated with aggressive behavior.

- The mismatch repair (MMR) deficient cases often show mixed morphology, with clear cell and endometrioid components .

- Clear cell ECs are typically negative for estrogen receptor protein and positive for Napsin A, which can aid in distinguishing this form of high-grade carcinoma from its mimics: SEC and the secretory variant of endometrioid EC

CLINICAL PRESENTATION

- **Abnormal uterine bleeding**
- **Abnormal cervical cytology**
- **Incidental finding on imaging**
- **Incidental finding after hysterectomy or during abdominopelvic surgery**

Tumor markers

- Elevated levels of CA 125 are associated with:
- Advanced stage,
- Poorly differentiated endometrioid adenocarcinomas
- Uterine serous cancers
- Uterine clear cell cancers

- ✓ **Elevations of CA 125 are associated with positive pelvic node involvement, positive peritoneal washings, and the presence of lymphovascular invasion .**

- ✓ **the prognostic effect of an elevated CA 125 on progression-free survival remains controversial .**

- ✓ **correlation between elevated CA 125 preoperatively and lymph node metastases was noted without association with development of recurrent disease**

prognosis

- Type II**: poorer outcome** than type I in most studies
- The five year disease specific survival rate for USC:55%
- clear cell carcinoma:68%
- Even among women with completely surgically staged ,node negative ,stage I, USC the five year disease specific survival rate is 70%.
- Women with clear cell carcinoma have similar prognosis the five year disease specific survival rate is 62.5%.

Thanks for your attention