For the last two decades, endometrial carcinoma has been subdivided into two major types (types I and II) based on epidemiology, conventional histopathology, and clinical behavior. Type I, which comprises approximately 80% of endometrial carcinomas newly diagnosed in the Western world, occurs predominantly in pre- and peri-menopausal women under unopposed estrogenic stimulation. These tumors are endometrioid carcinomas (EECs) that morphologically resemble normal endometrium and are frequently preceded by endometrial hyperplasia. They are usually confined to the uterus, exhibit low histological grade, and most patients are cured by hysterectomy. In contrast, type II endometrial carcinomas develop mainly in older post-menopausal women in whom the non-neoplastic endometrium is atrophic. These tumors are non-endometrioid carcinomas (NEECs), predominantly high grade serous or clear cell carcinomas, which are not associated with estrogen effect and are thought to derive from a malignant lesion designated ‘intraepithelial carcinoma’. Frequently, NEECs invade deeply into the myometrium and follow an aggressive clinical course. Also, it has been found that the genetic alterations carried by EECs differ from those of NEECs. Most were selected by analogy with colon cancer and were confirmed afterwards to occur in endometrial carcinoma. Recently, gene expression profiling has further expanded our knowledge of early genetic events and reinforced the clinicopathological subgroups originally defined by morphological and clinical features. However, even if a dualistic model may apply to typical cases, there is often overlap in the clinical, histopathological, immunohistochemical, and genetic characteristics of the tumors. Most endometrial carcinomas that are found in an atrophic endometrium are EECs, with a prognosis intermediate between the two types described above. Furthermore, it has been shown that some NEECs may develop from preexisting EECs as a result of tumor progression and, in such cases, the tumors may share histological and molecular features.

Women with an inherited predisposition for endometrial neoplasia tend to develop the disease 10 years earlier than the general population and have a favorable prognosis. Most of these patients have hereditary non-polyposis colorectal carcinoma (HNPCC), an autosomal dominant disorder due to germline mutations in one of the DNA mismatch repair (MMR) genes. Although colorectal cancer predominates, endometrial carcinoma occurs in 30–60% of cases.

References


ENDOMETRIAL CARCINOMA:
CLASSIFICATION AND GENERAL FEATURES

Jaime Prat, M.D., Ph.D., FRCPath.
Hospital de la Santa Creu i Sant Pau
Autonomous University of Barcelona, Spain
Endometrial Carcinoma

- Most common FGT cancer in western world
- 4th most common cancer in women (6%)
- Only 2% of cancer deaths in women
- Postmenopause (75%)
The two types of Endometrial Carcinoma

<table>
<thead>
<tr>
<th></th>
<th><strong>Type I</strong></th>
<th><strong>Type II</strong></th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Pre- and Perimenopausal</td>
<td>Postmenopausal</td>
</tr>
<tr>
<td><strong>Unopposed Estrogen</strong></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Hyperplasia-Precursor</strong></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td><strong>Myometrial Invasion</strong></td>
<td>Minimal</td>
<td>Deep</td>
</tr>
<tr>
<td><strong>Histologic Type</strong></td>
<td>Endometrioid</td>
<td>Nonendometrioid</td>
</tr>
<tr>
<td><strong>Behavior</strong></td>
<td>Stable</td>
<td>Progressive</td>
</tr>
<tr>
<td><strong>Genetic alterations</strong></td>
<td>Microsat Instability</td>
<td>P53 mutations, LOH</td>
</tr>
</tbody>
</table>

Modif from Bokhman JV. Gynecol Oncol 1983
Type I
Endometrial Carcinoma

Endometrioid

Non-Endometrioid

Catasús Ll. et al.
Hum Pathol 1998
Endometrioid Ca

Serous Ca
Catasús LI, et al.
Hum Pathol 1998