Relationship between microcystic, elongated, and fragmented pattern of myometrial invasion and histopathological prognostic factors in endometrioid endometrial carcinoma

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• I have no actual or potential conflict of interest in relation to this presentation.
Introduction

- Endometrial cancers are the most common cancer of gynecological malignancies*
  the second most common cause of death
- Its most common histologic subtype is endometrioid endometrial carcinoma (EEC)
- EEC generally has a favourable prognosis
- Recurrence and disease-related death also had been recorded
- Specific indicators are needed to determine high-risk patients, management and improve survival rates

Microcystic, Elongated, and Fragmented (MELF) pattern is one of the myometrial invasion patterns in EEC

Firstly described by Murray et al in 2003*

It is characterized by microcysts lined by cells that often have conspicuous eosinophilic cytoplasm and appeared squamoid, elongated structures, with a compressed, sometimes slit-like lumen edematous or myxoid tissue with retraction artifact and inflammatory cells

*Murray SK, Young RH, Scully RE. Unusual epithelial and stromal changes in myoinvasive endometrioid adenocarcinomas: a study of their frequency, associated diagnostic problems, and prognostic significance. Int J Gynecol Pathol 2003; 22; 324-33.
Introduction-3

- Fragmentation may result in small clusters of cells or single cells
- When only single cells present, it can be easily overlooked
- Can cause under-staging and undertreatment
- Its recognition is important for accuracy of measurement of myometrial invasion
- The characteristic flattened epithelium of MELF can imitate vascular endothelia
- It can mimic lymphovascular space invasion (LVSI)
Introduction-5

• MELF pattern has been observed to vary 9–43%*
• It is reported to be associated with deep myometrial invasion, cervical stromal invasion, LVI and lymph node metastasis*
• It has been proposed as a potential prognostic factor
• It remains uncertain as to whether the presence of MELF pattern has a clinical significance, because of the limited number of studies

Objective

• The purpose of this study:
  Examine the frequency of MELF pattern
  Relationship between MELF pattern with histopathological parameters in EEC
Methods-1

• 285 patients with EEC who underwent total hysterectomy and bilateral salpingo-oophorectomy with or without lymphadenectomy (January 2009 - December 2014) were included in this study

• Cases confined to the endometrium were excluded (n=52)

• A total of 233 cases with myometrial invasion were re-evaluated on H&E slides
Methods-2

• The presence or absence of MELF pattern,
• Clinicopathological data were recorded

• The association of MELF pattern with was analysed statistically with comparison of MELF positive and negative cases

• For statistical analyses, “IBM SPSS Statistics 24.0 trial version" were used. To compare qualitative/quantitative parameters, Mann-Whitney test, Fisher’s exact test, Pearson Chi-Square test were used
• p<0.05 was considered statistically significant

✓ age
✓ tumour grade
✓ depth of myometrial invasion
✓ presence of LVSI
✓ cervical stromal invasion
✓ lymph node metastasis
✓ FIGO stage (2009)
Results-1

- The frequency of MELF pattern was 21.8% (n=51)
- MELF pattern was frequently observed in the deepest* extent of invasion
The mean age was 60.8 (33-83)

There was no relation between age and presence of MELF statistically

<table>
<thead>
<tr>
<th>MELF pattern</th>
<th>Total n=233</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present n=51</td>
<td>Absent n=182</td>
<td></td>
</tr>
<tr>
<td>Age, mean±SD</td>
<td>62.5±9.1</td>
<td>60.3±9.1</td>
</tr>
</tbody>
</table>

aMann-Whitney test
Results-3

- Grade 1, 2 and 3 were seen 55%, 43% and 2% respectively in MELF positive cases.
- There was no relationship between grade and MELF pattern statistically (p=0.206).
Deep myometrial invasion was observed in 64% of MELF positive cases (n=33).

It was found to be statistically related with the presence of MELF (p=0.000).

<table>
<thead>
<tr>
<th>Depth of myometrial invasion</th>
<th>MELF +</th>
<th>MELF -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myometrial invasion &lt;50%</td>
<td>18</td>
<td>121</td>
</tr>
<tr>
<td>Myometrial invasion ≥50%</td>
<td>33</td>
<td>61</td>
</tr>
</tbody>
</table>
• LVSI was present in 23% of MELF positive cases (n=12)

• There was significant relationship between LVSI and the presence of MELF (p=0.021)
• Cervical stromal invasion was seen in 17% of MELF positive cases (n=9)

• Relationship between cervical stromal invasion and MELF was not statistically significant (p =0.126)

<table>
<thead>
<tr>
<th></th>
<th>MELF +</th>
<th>MELF -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Absent</td>
<td>42</td>
<td>164</td>
</tr>
</tbody>
</table>
Results

- Lymphadenectomy was performed in 212 patients
- In 26 cases lymph node metastasis was observed
- LN metastasis was present in 19% of MELF positive cases (n=10)
- There was significant relationship between LN metastasis and MELF statistically (p=0.027)
Results

- Advanced FIGO stage was seen in 19% of MELF positive cases (n=10)
- It was found to be statistically significant with MELF pattern (p=0.043)

<table>
<thead>
<tr>
<th>FIGO stage distribution</th>
<th>MELF +</th>
<th>MELF -</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIGO I-II</td>
<td>41</td>
<td>165</td>
</tr>
<tr>
<td>FIGO III-IV</td>
<td>10</td>
<td>17</td>
</tr>
</tbody>
</table>
Discussion

- Ten studies reported that patients with LN metastasis were more likely to be MELF\textsuperscript{1-10}
- Five studies reported that LVSI was likely to be related with MELF\textsuperscript{1,2,4,5,11}
- Three studies detected that deep myometrial invasion was related with MELF\textsuperscript{2,4,11}, whereas 1 found no difference\textsuperscript{1}
- Relationship between MELF pattern and advanced FIGO stage was significant in two studies\textsuperscript{2,4}
  - Our study showed that MELF pattern is related with LN metastasis, LVSI, deep myometrial invasion and advanced FIGO stage
Discussion

• Two studies proved that MELF was related with cervical stromal invasion\textsuperscript{1,4}, whereas 1 found no difference\textsuperscript{2}.

• Three studies found no difference between age and MELF\textsuperscript{1,2,4}, only 1 study found significant relation\textsuperscript{11}.

• One study reported that MELF was related with high grade tumours\textsuperscript{11}, while 1 indicated relation with low grade tumours\textsuperscript{4}.

• One study found no difference with tumour grade\textsuperscript{1}.
  ➢ Our study showed that MELF pattern had no relation with age, grade and cervical stromal invasion.
Conclusion

• The overall incidence of MELF in this study is 21.8%

Statistically significant

➢ Deep myometrial invasion
➢ Presence of LVSI
➢ Lymph node metastasis
➢ Advanced FIGO stage

Not statistically significant

➢ Age
➢ Tumour grade
➢ Cervical stromal invasion

• This findings are correlated with various studies
Conclusion

• The limitation of this study is it has no data about survival and recurrence
• This study is a preliminary result and will be improved by adding the above data
References


Thank you so much for your patience 😊