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Microcystic, Elongated, and Fragmented (MELF) Pattern Invasion in Ovarian Endometrioid Carcinoma: Immunohistochemical Profile and Prognostic Implications

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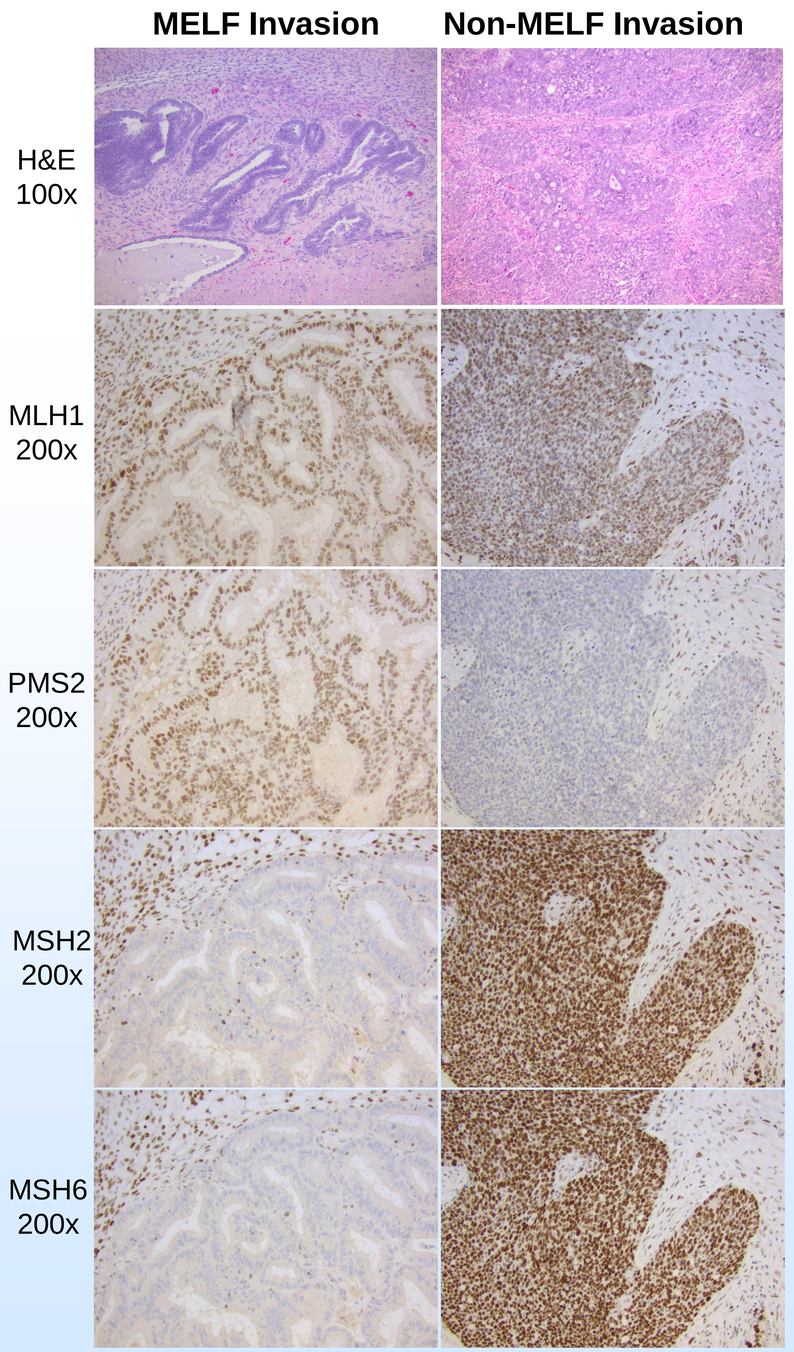
BACKGROUND

- Microcystic, Elongated and Fragmented (MELF) is a well-recognized pattern of uterine endometrioid carcinoma (UEC) associated with lymphovascular space invasion and occult lymph node metastasis
- MELF in UEC may be seen with Lynch Syndrome
- MELF in UEC is hypothesized to be histologic evidence of an epithelial mesenchymal transition
- MELF pattern invasion in ovarian endometrioid carcinoma (OEC) was first described at USCAP 2015
- Current study evaluates MELF in OEC for
  - Prognostic implications
  - Immunohistochemical (IHC) profile related to
    - Lynch Syndrome
    - Epithelial mesenchymal transition

DESIGN

- 42 consecutive cases of OEC without concurrent UEC (1996-2014) evaluated by 2 pathologists
- MELF defined as at least three glands fulfilling histologic criteria
- 32 cases had blocks available for staining
  - MLH1, PMS2, MSH2 and MSH6 for mismatch repair (MMR) protein expression
    - Graded as “retained” or “lost”
  - β-catenin, e-cadherin, CK19 and cyclin D1 for evidence of epithelial mesenchymal transition
    - Graded as “rare” (<25% cells stain), “moderate” (25-75% cells stain), or “strong” (>75% cells stain)
- Retrospective chart review of clinical and demographic features and overall survival
- Data analyzed using Fisher exact test analysis
- Survival analyzed using Kaplan-Meier method



RESULTS

- MELF pattern invasion was identified in 45% of the cases reviewed
- Clear cell features were only seen in cases with MELF pattern invasion (p-value=0.044)
- Overall, 13% of cases demonstrate MMR protein loss
  - MELF: MSH2/MSH6 deficiency (n=2)
  - Non-MELF: PMS2 deficiency (n=2)
- No difference was identified in:
  - Overall survival
  - Cancer recurrence
  - IHC staining for β-catenin, e-cadherin, CK19 and cyclin D1
  - Serous features
  - Concurrent endometriosis
  - Lymphovascular space invasion
  - Lymph node metastasis
  - Bilaterality of disease
  - Extranodal metastasis

CONCLUSIONS

- MELF occurs in ovarian endometrioid carcinoma at a similar or higher frequency than in uterine endometrioid carcinoma.
- Clear cell features were identified exclusively in MELF pattern invasion cases.
- Different MMR proteins are lost in MELF and non-MELF pattern invasion carcinomas.
- As there is no current consensus on Lynch screening in patients with ovarian endometrioid carcinoma, perhaps the presence of MELF pattern invasion should prompt screening.
- MELF should be considered when assessing ovarian endometrioid carcinoma, as the pattern may be confused with endometriosis or endosalpingiosis.