2022-RA-947-ESGO BI ALLELIC LOSS OF MSH2 IN ENDOMETRIAL CARCINOMA, A CASE REPORT

[1]Aisling E Redmond, [2]Rory Kennelly, [3]Donal J Brennan. [1]*Obstetrics and Gynaecology, National Maternity Hospital, Dublin, Ireland*; [2]*Colorectal Surgery, St. Vincent's University Hospital, Dublin, Ireland*; [3]*UCD Gynaecological Oncology Group, University College Dublin, Dublin, Ireland*

10.1136/ijgc-2022-ESGO.263

Introduction/Background Microsatellite instability plays an important role in the development of sporadic endometrial cancer. Mutations in mismatch repair proteins lead to MSI which leads most commonly to somatic hypermethylation and inactivation of MLH1-gene.

Methodology We report a case of endometrioid endometrial adenocarcinoma (EAC) which demonstrated a 'double hit' or bi-allelic somatic inactivation of MSH2-gene.

Results A 56 yo nulliparous lady presented with post-menopausal bleeding. Histology of endometrial curretings confirmed grade one EAC, estrogen receptor positive, p53 wild type and MMR deficient. CT-TAP was negative for metastasis. Patient underwent total laparoscopic hysterectomy and bilateral salpingoophorectomy. Sentinel lymph node mapping was unsuccessful however intra-operative assessment demonstrated myometrial-invasion <50%, and comprehensive pelvic lymph node dissection was deemed unnecessary. Post-operative histology gave a stage of FIGO 1a, pT1aNxMo, Grade 1 EAC. The was no LVSI/cervical stroma/adnexal/parametrial involvement. MMR-immunohistochemistry demonstrated loss of MSH2 and MSH6 suggestive of Lynch syndrome (LS), however germline testing failed to identify any abnormality. Further somatic testing identified two independent presumed somatic pathogenic MSH2 mutations. This reduces likelihood of LS and presented an extremely rare case of double somatic mutation of MSH2-gene.

Conclusion MMR gene alterations (hMLH1/hMSH2) play an important role in the development of MSI in sporadic EAC. Most presumed sporadic, MSI-positive EACs are associated with epigenetic silencing of *MLH1*, via promoter hypermethylation. A smaller fraction have somatic mutations in *MSH6*, or loss of MSH2 protein expression. Hereditary cancers can also display mutations in MSH2-gene. LS is an autosomal dominant hereditary cancer syndrome which increases cancer risk, most notably colorectal and endometrial. It is caused by germline mutations in MMR genes – MSH1/MSH2/MSH6/PMS2 and EPCAM-genes. ~36% of MMR deficient EAC are caused by LS. Here we report a case of EAC demonstrating a 'double hit' or bi-allelic somatic inactivation of MSH2-gene highlighting the importance of complete clinical algorithms in these cases.

2022-RA-955-ESGO ENDOMETRIAL CANCER: LYMPHOVASCULAR SPACE INVASION IS A NEGATIVE PROGNOSTIC FACTOR

[1]Alixe Salmon, [2]Adriane Dheur, [3]Vincent Bours, [4]Katty Delbecque, [1]Elodie Gonne, [5]Clemence Pleyers, [2]Marjolein de Cuypere, [2]Frederic Goffin, [6]Pierre Lovinfosse, [2]Frederic Kridelka, [2]Athanasios Kakkos, [1]Christine Gennigens. [1]*Oncology, CHU Liège, Liege, Belgium*; [2]*Gynaecology and Obstetrics, CHU Liège, Liege, Belgium*; [3]*Human Genetics, CHU Liège, Liege, Belgium*; [4]*Pathology, CHU Liège, Liege, Belgium*; [5]*Radiation Oncology, CHU Liège, Liege, Belgium*; [6]*Nuclear Medicine and Oncological Imaging, CHU Liège, Liege, Belgium*

10.1136/ijgc-2022-ESGO.264

Introduction/Background Endometrial carcinoma (EC) is the most common cancer of the female genital tract in developed countries. Lymphovascular space invasion (LVSI), an histological characteristic, is also included in the molecular classification. We aimed to compare the clinical profile but also overall survival (OS) and progression-free survival (PFS) in patients with and without LVSI.

Methodology Between January 2019 and December 2021, we conducted a monocentric retrospective study of 166 patients treated for EC (all stages) at the CHU of Liège. Thirty-nine patients were excluded. Data of the 127 remaining patients were analyzed for quantification of LVSI: absence, rare (< 5), substantial (≥ 5) or lymphangitis. The statistical correlation between the LVSI status and various clinical (FIGO stage, lymph node invasion, histological type and grade) and molecular factors was assessed using chi-square and Fisher's exact tests. Kaplan-Meier methods were used to determine OS and PFS.

Results 33.6% (n = 37/127) – 40.9% (n = 45/127) – 21.8% (n = 24/127) and 3.6% (n = 4/127) have absence, rare, substantial LVSI and lymphangitis, respectively. There is a significant correlation between the presence of LVSI (LVSI+) and higher grade (p=0.0001) but also with lymph node invasion (12.2% vs 0%, p=0.046). OS at 24 months was 96% and 82% in LVSI – and LVSI + cohorts, respectively (HR = 2.59, p=0.37).

Regarding molecular analyses, more patients with LVSI+ have microsatellite instability (42.7% vs 16.2%, p=0.0045). No significant correlation was found between the LVSI quantification and p53 mutation, POLE status or histological subtype.

Conclusion The presence of LVSI is a negative prognostic factor, with aggressive features, but without statistically reduction in OS. However, concerning absolute values, the presence of LVSI demonstrates worse prognosis. A significant association with microsatellite instability is demonstrated. The LVSI status should systematically be determined to optimally define the patient prognosis.

2022-RA-963-ESGO THE IMPACT OF LOW-VOLUME METASTASIS ON DISEASE-FREE SURVIVAL OF WOMEN WITH APPARENT EARLY-STAGE ENDOMETRIAL CANCERUNDERWENT SENTINEL NODE BIOPSY: A RETROSPECTIVE STUDY

[1]Alessandro A Buda, [2]Cristiana Paniga, [3]Salih Taskin, [4]Michael Mueller, [5]Ignacio Zapardiel, [6]Francesco Fanfani, [7]Andrea Puppo, [8]Andrea Papadia, [9]Elena de Ponti, [10]Hasan Turan, [1]Stefania Perotto, [11]Mete Gungor, [3]Firat Ortac, [4]Sara Imboden, [12]Fabio Ghezzi, [6]Giovanni Scambia, [13]Cagatay Taskiran, [2]Robert Fruscio. [1]*Gynecology Oncology Unit, Ospedale Michele e Pietro Ferrero, Verduno, Italy*; [2]*Obstetrics and Gynecology, University of Milano-Bicocca, San Gerardo Hospital, Monza, Italy*; [3]*Obstetrics and Gynecology, Ankara University School of Medicine, Ankara, Italy*; [4]*Obstetrics and Gynecology, Inselspital, University Hospital of Bern and University of Bern, Bern, Switzerland*; [5]*Gynecologic Oncology Unit., La Paz University Hospital, Madrid, Spain*; [6]*Obstetrics and Gynecology, Fondazione Policlinico Universitario A. Gemelli IRCCS Università Cattolica del Sacro Cuore, Roma, Italy*; [7]*Obstetrics and Gynecology, Ospedale Santa Croce e Carle, Cuneo, Italy*; [8]*Department of Gynecology and Obstetrics, Ente Ospedaliero Cantonale, University of the Italian Switzerland, Lugano, Switzerland*; [9]*Department of Physical Medicine, University of Milano-Bicocca, San Gerardo Hospital, Monza, Italy*; [10]*Department of Obstetrics and Gynecology, University of Health Sciences, İstanbul Training and Research Hospital, İstanbul, İstanbul, Turkey*; [11]*Department of Obstetrics and Gynecology, Acibadem University School of Medicine, İstanbul, Istanbul, Turkey*; [12]*Department of Obstetrics and Gynecology, 'Filippo Del Ponte' Hospital, University of Insubria, Varese, Italy*; [13]*Department of Obstetrics and Gynecology, Koc University School of Medicine, Istanbul, Turkey*

10.1136/ijgc-2022-ESGO.265