#980 MLH1 PROMOTER HYPERMETHYLATED ENDOMETRIAL CANCER: CLINICAL AND MOLECULAR CHARACTERISTICS FROM A RETROSPECTIVE COHORT

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Introduction/Background MLH1 promoter hypermethylation is common in sporadic microsatellite unstable endometrial cancer but data on MLH1 promoter hypermethylated endometrial cancer (MLH1-PM EC) is sparse. We aimed to identify the clinical and molecular characteristics of MLH1-PM EC.

Methodology Descriptive analysis of 246 tumours from patients treated between September 2007 to June 2022. Mismatch repair proteins (MMR) were tested by immunohistochemistry (IHC). Tumour specimens were sequenced using the Royal Marsden RMH200Solid panel which includes 233 genes and evaluates microsatellite instability (MSI) and tumour mutational burden (TMB). Droplet Digital PCR (ddPCR) was used for DNA methylation analysis in each case. Patients' characteristics were recorded from our electronic records.

Results MLH1-PM was identified in 71/246 tumours (28.9%): 61 were MMRd and 10 MMR proficient by IHC. The most common protein loss was MLH1/PMS2 in 57/61 cases (93.5%). Isolated loss of MSH6 was present in 3 cases and MSH2/MSH6 loss in 1 case. MLH1-PM tumours were MSI high in 47/71 (66.2%) of cases with a mean TMB of 30.96 mut/mb (12.21–193.93) and MSS in 24/71 (33.8%) of cases with a mean TMB of 48.65 mut/mb (0–231.91). The predominant histological subtype was endometrioid (n=64). Most tumours were stage I or II at diagnosis (n=55). Mean age at diagnosis was 65 years (32–90) and mean body mass index (BMI) was 31.64 (17.3–53.9). 14/71 (19.7%) patients presented with relapsed disease after initial diagnosis: locoregional in 4 cases and systemic in 10 cases. Genomic analysis revealed that MLH1-PM ECs were enriched in PTEN, ARID1A, PIK3CA, KMT2D, KMT2C, PIK3R1, KRAS, FAT1, BCOR and ATM mutations. In patients who relapsed (n=14), gain of chromosome 1q was identified in 7 cases (50%).

Conclusion MLH1-PM EC is found in 30% of unselected EC patients and harbors genomic alterations that may have potential prognostic and therapeutic implications. Further studies are needed to develop appropriate treatment strategies.

Disclosures Dr. Alexandra Taylor: MSD.

Dr. Angela George : Astra Zeneca, GSK, Roche, Merck.

#991 EVALUATION OF CLINICAL AND PATHOLOGICAL DATA OF PATIENTS WITH ENDOMETRIUM CANCER WITH MICROSATELLIT INSTABILITY

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Introduction/Background To investigate the frequency and clinical significance of Microsatellite Instability (MSI) in endometrial cancer patients.

Methodology The study included 174 patients who underwent total hysterectomy with the diagnosis of endometrial cancer in Hacettepe University Hospital, Department of Obstetrics and Gynecology between January 1, 2019 and March 30, 2021. Loss of expression of DNA mismatch (MMR) proteins was investigated by pathological examination. Patients who were found to be at risk of Lynch syndrome as a result of MMR research were referred to the medical genetics department.

Results The median age of the patients was 60 (min: 35, max: 94). 83.9% of patients were postmenopausal (146/174). The median BMI of the patients included in the study was 30.2 (min: 19.0, max: 54.1). Early stage endometrial cancer was observed in the vast majority of patients (Stage 1A: 54.6%). In the final pathology results, endometrioid adenocarcinoma was the most common with 81%, and serous type cancer was detected in 8% of the patients.

All pathological specimens were analyzed for MMR gene defect. MMR loss was detected in 35.1% of the patients (61/174). The relationship between MMR loss status and histological type is summarized in table 1. In addition, 11.5% (20/174) of the patients in our study were found to be p53 mutants.

Conclusion Today, molecular classification plays a role in the adjuvant treatment plan and prognosis predictions of endometrial cancer. Patients with MMR gene defect, which constitutes 25–30% of endometrial cancers, should be evaluated in terms of Lynch syndrome. In our study, it was found that MMR gene defect is more common in endometrioid type and mixed type endometrial cancers, in line with the literature. Longer follow-up is required for interpretation of survival data.

Abstract #991 Table 1 Relationship between MMR Loss and Histological Type

Histological Type	MMR Loss	
	YES	NO
Endometrioid	56	84
Mix	2	3
Carcinoma	0	5
Mucinous	0	2
Serous	0	14
Clear	0	3
Dedifferentiated	3	1

Disclosures .The authors have no conflict of interest related this research

#993 SURVIVAL OUTCOMES OF PATIENTS WITH INOPERABLE ENDOMETRIAL CANCER TREATED WITH RADICAL RADIOTHERAPY

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Introduction/Background Endometrial cancer is the most frequently treated gynaecological cancer. The current standard of care of endometrial cancer involves resection, often followed by adjuvant treatment with radiotherapy or chemotherapy. However, some patients may not be candidates for surgery and require alternative treatment options, such as radiotherapy.