BI ALLELIC LOSS OF MSH2 IN ENDOMETRIAL CARCINOMA: A CASE REPORT

Introduction/Background

Microsatellite instability plays an important role in the development of sporadic endometrial cancer. Mutations in mismatch repair proteins lead to MSI with epigenetic silencing 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 curettings 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 salpingo-oophorectomy. 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.

THE IMPACT OF LOW-VOLUME METASTASIS ON DISEASE-FREE SURVIVAL OF WOMEN WITH APPARENT EARLY-STAGE ENDOMETRIAL CANCER UNDERWENT SENTINEL NODE BIOPSY: A RETROSPECTIVE STUDY

Introduction/Background

Endometrial carcinoma (EC) is the most common cancer of the female genital tract in developed countries. Lymphovascular space invasion (LVI), 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 LVI.

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 LVI: absence, rare (< 5), substantial (≥ 5) or lymphangitis. The statistical correlation between the LVI 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 LVI and lymphangitis, respectively. There is a significant correlation between the presence of LVI (LVI+) 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 LVI+ and LVI + cohorts, respectively (HR = 2.59, p=0.37).

Conclusion

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