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"Survival of Mismatch Repair Deficient Endometrial Cancer in a Black population"

Introduction: Minority women, particularly Black women, are disproportionately affected by the effects of endometrial cancer (EC), with approximately one-third exhibiting defects in the DNA Mismatch Repair (MMR) pathway, characterized by deficiencies in MMR proteins (MSH2, MLH1, PMS1, and PMS2) detected via immunochemistry. MMR deficiency leads to the accumulation of DNA base pair mismatches and genomic alterations, ultimately resulting in carcinoma. Loss of MMR can be acquired from hereditary loss, such as that seen with Lynch syndrome, and/or acquired in a sporadic pathway, most commonly by epigenomic hypermethylation of MLH1. Despite this, the impact of mismatch repair deficiency (MMRd) and its role in the Minority EC population is poorly understood. This study aimed to observe the prognostic value of hereditary or sporadically acquired MMRd about presentation and survival within the Minority EC population in southwest Louisiana.

Methods: We conducted a retrospective cohort study of minority EC patients who underwent MMR testing and received care with LSUHSC-associated gynecologic oncologists (2018-2023). A comprehensive chart review was performed to extract patient demographic, clinicopathologic, and survival data. Collected data was entered and stored into a REDCap database; statistical analysis was employed for summary statistics and pairwise comparisons to determine if there are significant differences in stage, grade, and histology of presentation based on the mode of acquisition of MMRd for Minority EC patients.

Results and Conclusion: Among 200 reviewed patient charts for individuals identifying as African Americans with EC patients, N=15 (7.50%) exhibited MMRd. The median age was 60 years at diagnosis. Most patients, n=14 (77.7%), presented with sporadic MMRd characterized by mutation across 22 genes. Several patients exhibited concurrent mutations in multiple MMR genes, such as simultaneous mutations in MLH1 and PMS2. Consequently, the most frequently affected MMR genes were PMS2 (n=11, 84.6%), MLH1 (n=10, 76.9%), and MLH2 (n=1, 7.7%). Only one patient within this cohort demonstrated hereditary MMR loss, specifically in the PMS2 gene. In situations of absent MMR function, 53.28% (n=7) presented with hypermethylation of the MLH1 promoter. Among the 15 MMRd patients, 66.70% (n=10) presented with Early-Stage EC (Stage I or II), and 33.4% (n=5) presented with Advanced-Stage (Stage III or IV). Histologically, 40.0% of cases were classified as Grade 1 EC (n=6), 26.7% as Grade 2 (n=4), 20.0% as Grade 3 (n=3), and 13.4% were not reported or classified as "other" (n=2). Collectively, 80.0% of our population presented with histology indicating Endometrioid Adenocarcinoma (EAC) (n=12), while both Carcinosarcoma and Uterine Papillary Serous Carcinoma each accounted for 13.3% of the cases (2 cases each). 20.0% (n=3) were classified as "cancer not otherwise specified," and another 20.0% (n=3) were categorized as "other." 73.3% of patients (n=11) are alive with no evidence of disease, 13.3% are alive with disease (n=2), and 13.3% died from cancer-related reasons (n=2). This study aims to uncover survival differences among minority women with MMRd endometrial cancer based on acquisition patterns. Due to limited sample sizes, reporting specific outcomes by race and ethnicity may not be feasible.