CORRELATION OF MISMATCH REPAIR DEFICIENCY WITH HISTOPATHOLOGICAL SUBTYPES AND CLINICAL OUTCOME IN ENDOMETRIAL CANCER

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Introduction

Endometrial carcinoma (EC) is the most common uterine cancer and the second most frequent gynecological malignancy in Egypt and Worldwide. With the recognition of its four molecular subtypes, EC treatment strategies have changed globally, and molecular profiling is now an essential part of clinical judgment, especially for patients with POLE and p53 mutations. Contrary, Mismatch Repair Deficiency (MMRd) being the second most common and aggressive subtype of EC due to its heterogeneity, its clinical features and oncological outcomes remain controversial worldwide. In North Africa and Africa in general not only the behavior of MMRd group is disagreeable but also we still have a crucial knowledge gap regarding EC molecular profiling which is highlighted by lack of data.

Aim of the work

To correlate MMRd and clinicopathological factors in endometrial cancer (EC) and assess the impact of MMRd on oncological outcomes in EC patient.

Methods

This retrospective study included 43 patients diagnosed with endometrial cancer and treated at the Alexandria Clinical Oncology Department between 2020 and 2022. MMR status was assessed using immunohistochemistry, and the results were statistically correlated with clinical presentation, tumor pathological characteristics, and patient outcomes.

Results

This study involved 43 endometrial cancer patients, aged 29-73 (median 60). MMRd was present in 17 patients (39.5%), with 15 showing MLH1/PMS2 loss, 1 with MSH2/MSH6 loss, and 1 with isolated MSH6 loss. p53 mutations were found in 30.2% of cases. No significant correlations were observed between MMRd and age (p:0.576), histological subtype (p: 0.821), grade (p: 0.432), stage (p: 0.07), myometrial invasion (p:0.176) or LVSI (p: 0.101). The 48-month recurrence-free survival (RFS) was 92.3% in the MMRp group and 94.1% in the MMRd group. The lowest RFS was seen in the MMRp-p53 mutated group (77%), whereas p53 status had no impact on recurrence in the MMRd group. The overall survival (OS) at 48 months was 93% for all patients, with 7% of deaths occurring in the MMRp-p53 mutated group. The MMRd group had a 100% OS, with no effect of p53 status on survival in this cohort.

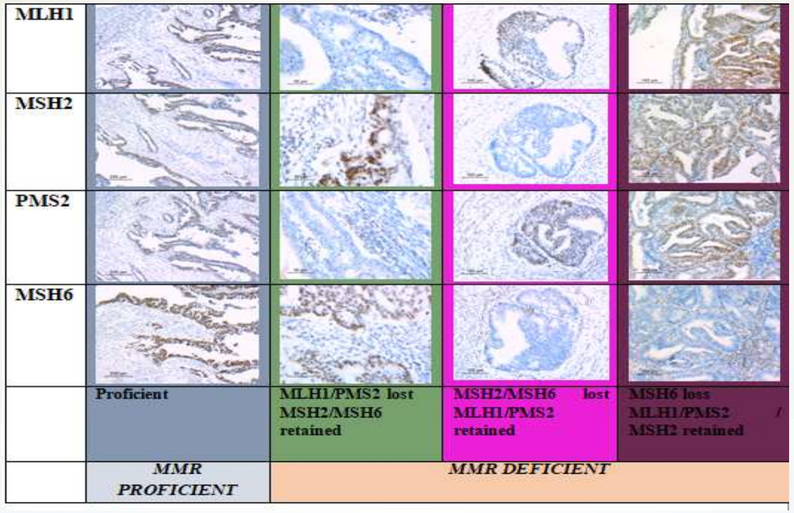

Figure 1: MMR protein expression

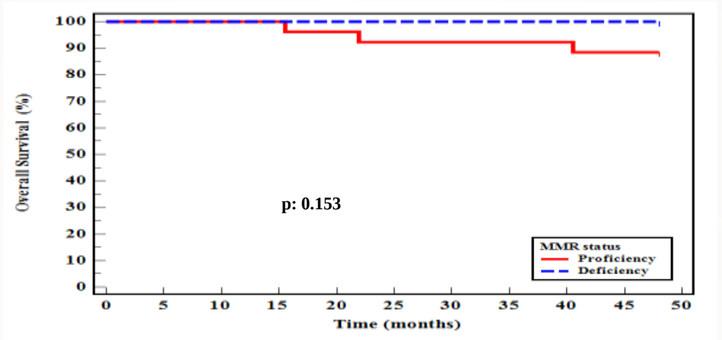

Figure 2 : Kaplan-Meier overall survival curves for patients with MMRd and MMRp

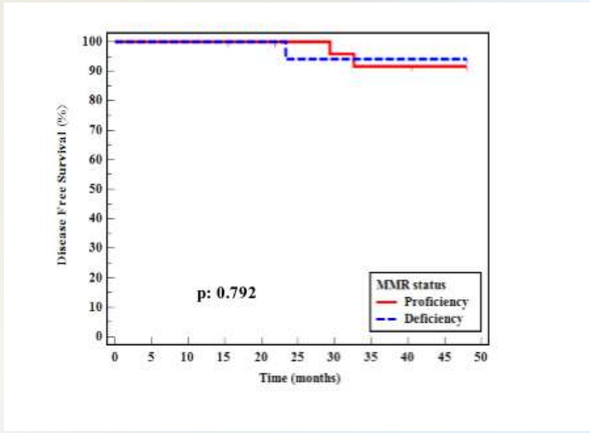

Figure 3 : Kaplan-Meier recurrence free survival curves for patients with MMRd and MMRp

Conclusion

We recommend routine testing of MMR proteins alongside p53 before treatment escalation in settings where the whole EC molecular profiling is not affordable. Additionally, further research with larger sample sizes on endometrial cancer in North Africa is crucial to validate international findings and improve test accessibility for African populations.recommend routine testing of MMR proteins alongside p53 before treatment escalation in settings where the whole EC molecular profiling is not affordable. Additionally, further research with larger sample sizes on endometrial cancer in North Africa is crucial to validate international findings and improve test accessibility for African populations.