Molecular and clinicopathological analysis of ovarian carcinomas with and without microsatellite instability

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BACKGROUND: Microsatellite instability (MSI) occurs in sporadic ovarian carcinomas. This study tests the hypothesis that ovarian carcinomas arising through the mutator pathway have distinctive clinical and molecular features that affect clinical outcome. MATERIALS AND METHODS: The MSI status was evaluated in 66 ovarian carcinomas and 11 epithelial ovarian tumors of low malignant potential. For the analysis with the microsatellite markers, a fluorescence-based PCR method was employed and the prognostic significance of the MSI status was assessed. DNA copy number changes in tumors with and without MSI were analyzed by comparative genomic hybridization. RESULTS: High-frequency MSI (MSI-H) was found in 30% of the carcinomas, whereas low-frequency MSI (MSI-L) occurred in 32%. In LMP tumors, only MSI-L was detected (18%). There was a trend for tumors with MSI-H and MSI-L to have a poor prognosis, but this relationship did not reach significance (p=0.09 and p=0.07, respectively). MSI-H in carcinomas was significantly associated with poor differentiation (p=0.03) and higher clinical stage (p=0.03). No correlation was found between different histological types of ovarian carcinoma and the microsatellite status. In a multivariate analysis, MSI at the dinucleotide repeat D5S346 was found to be of independent prognostic significance (p<0.008) for disease-specific survival. There was no association between the total number of genetic aberrations per tumor and the MSI status. CONCLUSION: Microsatellite instability is a relatively common event in ovarian carcinoma. The data indicate that instability of a single microsatellite marker on chromosome 5 (D5S346) might be indicative of disease progression when detected in early clinical stages.

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