Abstract:
A major molecular pathway of genetic instability in cancer is DNA mismatch repair deficiency, leading to accumulation of numerous mutations at repetitive DNA sequence stretches (microsatellites), known as high-level microsatellite instability (MSI-H). In colorectal cancer, MSI-H tumors show a clinical behavior different from microsatellite-stable (MSS) tumors. Data about the prevalence of MSI among non-small cell lung cancer (NSCLC) are conflicting, and clinical relevance of MSI is largely unknown. We analyzed a series of 480 pulmonary adenocarcinomas (ADC) for MSI using a sensitive mononucleotide marker panel (BAT25, BAT26, and CAT25). Positive cases were further analyzed by immunohistochemical staining for DNA mismatch repair proteins. Results were correlated with clinicopathological variables. MSI-H was detected in 4/480 (0.8%) cases. In none of these, a background of Lynch syndrome was found. Three of the patients developed a metachronous carcinoma (esophagus, pancreas, and kidney). All MSI-H cases were stage I and occurred in smokers/ex-smokers. Mutations were found in EGFR (n = 2), KRAS (n = 1), or BRAF (n = 1). MSI-H neoplasms had a higher proliferative activity (38.7%) than MSS neoplasms (28.3%). Mean overall survival for MSS and MSI-H cases was 64.8 (CI...
60.4-69.1) and 47.1 (CI 21-73.2) months, respectively. When specific mononucleotide marker panels are applied, the MSI-H phenotype is rare and predominantly found in early stage ADC of smokers. However, the frequency of MSI-H is in the range of other relevant molecular alterations. In the era of precision therapy, associations with distinct clinicopathological variables merit further investigation.