구연발표 I-4

Aberrant Promoter Methylation Profile in Low- and High-Grade Gastric Lymphoma

Division of Gastroenterologic Surgery, Department of Surgery, Chonnam National University Medical School, Gwangju, Korea

Jae Kyoon Joo, Dong Yi Kim, Young Kyu Park, Seong Yeob Ryu, Young Jin Kim, Shin Kon Kim

Malignant lymphoma arising from mucosa-associated lymphoid tissue (MALT) accounts for a large proportion of extranodal lymphomas. The stomach is the usual site of MALT lymphoma, and the pathogenesis of gastric MALT lymphoma is closely related to Helicobacter pylori infection. Epigenetic silencing of tumor-related genes owing to CpG island methylation has recently been reported in B cell lymphomas, but its role in gastric lymphoma is unclear. Therefore, we analyzed the methylation status of cell cycle control (p16), apoptosis regulation (death-associated protein kinase, DAPK), and DNA mismatch repair (MGMT, hMLH1, and hMSH3) genes using the methylation-specific polymerase chain reaction in 46 cases of low- and high-grade gastric lymphoma. We found that p16, DAPK, and MGMT were more frequently methylated in high-grade lymphomas than in low-grade lymphomas (80, 80, and 93% vs. 71, 74, and 84%, respectively). Methylation of hMLH1 and hMSH3 was rare or absent. There were no differences in the frequencies of the CpG island methylator phenotype (CIMP) between low- and high-grade gastric lymphomas. Comparing the 46 gastric lymphomas with matched normal gastric mucosa, five had the microsatellite instability (MSI)-low phenotype, of which two were low-grade and three were high-grade lymphomas.

Our results suggest that the methylation of p16, DAPK, and MGMT represents a major pathogenic event in gastric lymphomas that may contribute to early tumorigenesis. This may have clinical application in the management and follow-up of low- and high-grade gastric lymphomas.