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Effect of Leptin Gene Methylation on Colorectal Cancer Chemoresistance

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Abstract : Colorectal cancer (CRC) is one of the most common tumors all over the world. Obesity, considered a risk factor of CRC, is characterized by a high level of secreted cytokines from adipose tissue. Among these inflammatory molecules, leptin is considered the key mediator for CRC cancer development and progression by activation of mitogenic and anti apoptotic signaling pathways. Gene expression can be significantly modulated by alterations in DNA methylation patterns. The aim of this study is to investigate the impact of leptin gene methylation on CRC prognosis and sensitivity to chemotherapy. The study involved 70 CRC tissue samples collected from King Abdullah University Hospital (KAUH) from which only 53 was analyzed because of bisulfate fragmentation and low yield of DNA extracted from FFPE tissues. A total of 22 blood samples were collected from healthy volunteers and enrolled as a control group. Leptin promoter methylation was analyzed by methylation specific PCR after bisulfate conversion. Results revealed that the incidence of leptin gene methylation was significantly higher in CRC patients in comparison to that of controls ($P < 0.05$). The correlation between patient's demographics and leptin gene methylation was not significant ($P < 0.05$). However, a significant correlation between leptin gene methylation status and early cancer stages (I, II and III) was found in male but not in female ($p < 0.05$). Moreover, a significant correlation was found between leptin promoter methylation and early tumor localization T1-2 ($p < 0.05$). The correlation between epigenetic regulation of leptin and chemosensitivity was not significant. Taken together, these results suggest the possibility to use leptin gene methylation as a biomarker for the evaluation of CRC prognosis and metastasis.

Keywords : colorectal cancer, obesity, leptin, DNA methylation, disease prognosis, bisulfate conversion, chemoresistance
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