ASSOCIATION BETWEEN METHYLATION OF THE HOXA10 HOMEBOX GENE PROMOTER AND ENDOMETRIAL CANCER: A CASE CONTROL STUDY.
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In this study we report the methylation profile of HOXA10 promoter gene in normal and malignant endometrial tissues. Given the role of HOXA10 in endometrial development it has been suggested that an aberrant hypermethylation of this gene could contribute to tumorigenesis. We collected 46 samples, 19 histological proven endometrioid cancers (EC) and 27 normal endometrial tissues (NET). In the NET group there were 14 proliferative endometrial tissues (PET) and 13 secretive endometrial tissues (SET). NET samples were processed by micromanipulation to separate glandular from stromal components. Glandular endometrial tissues (GET) and stromal endometrial tissues (StET) were analyzed separately. Genomic DNA was extracted from all tissue samples (EC, PET, SET, GET, StET) using an automated system (BioRobot EZ1, QIAGEN, Hilden, Germany). Methylation status in normal and malignant samples was expressed in percentage (+SD) of methylated sites in amplified region. Data were compared by one-way ANOVA test. Two-tailed P values less than 0.05 were considered significant. The mean methylation level of HOXA10 gene promoter in EC samples resulted 20.26+16.19. No significant association between methylation status and histological grading, deep infiltrating disease, extrauterine spread and survival was observed. The mean methylation levels of HOXA10 gene promoter in NET resulted as follows: GET=10.73+6.08, StET=8.04+6.98, SET=11.46+6.39, PET=8.33+5.93. No statistical difference was observed in mean methylation level among the subgroups of NET. On the contrary, differences in mean methylation values reached statistical significance between EC and all the subgroups of NET (EC vs GET=0.009, EC vs StET=0.001, EC vs PET=0.001; EC vs SET=0.015). These preliminary data showed that EC displayed significantly higher methylation status in HOXA10 gene promoter than normal tissue, suggesting a possible role of epigenetic changes in HOXA10 gene regulation in EC.