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Methylation of promoter region of BRCA1 gene versus pathogenic variants of gene: risk factor or clinical marker of breast cancer

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Abstract

Background: In this study, we compared the contribution of pathogenic variants of the BRCA1/2 genes (5382insC, 185delAG, 6174delT, 4153delA, T300G) and hypermethylation of the BRCA1 gene promoter region to the risk of breast cancer and clinical features in women.

Methods: This study enrolled 74 women (tumor tissue, blood) with newly diagnosed breast cancer and 62 women (blood) without oncological pathology (control group). Molecular genetic testing of samples and determination of hypermethylation status were performed on freshly collected material with the addition of a preservative before the procedure of DNA isolation.

Results: Hypermethylation of the BRCA1 gene promoter in women is a risk breast cancer factor (χ2 = 19.10, p = 0.001, OR = 16.25 (3.67-71.92)) and is more common than major pathogenic variants in the BRCA1/2 genes. The patients with the BRCA1 gene promoter hypermethylation were more likely to be diagnosed with late-stage metastatic cancer (χ2 = 4.31, p = 0.038, OR = 4.04 (1.19-13.65)). Hypermethylation of the BRCA1 gene promoter was predominant in tumor tissue among BC patients without family history compared to patients with cancer in relatives.

Conclusion: We proved that hypermethylation of the BRCA1 gene promoter is a risk factor for breast cancer and possibly an early biological marker of clinical onset, as its presence contributed to rapid disease progression with metastasis. The high frequency of hypermethylation in the examined breast cancer patients may be a consequence of environmental factors pressure on the risk of the disease development. Further large-scale studies are needed for the clinical application of the results.

Keywords: BRCA1; Breast cancer; Hypermethylation; Promoter; Tumor tissue.

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