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Congress Abstract

Spectrum of Germline Mutations in BRCA1 and BRCA2 Genes in Patients with Breast Cancer and Women with a Family History in the Kazakh Population

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Introduction: Germline mutations in the BRCA1 and BRCA2 genes are an important hereditary risk factor for the development of breast cancer. The spectrum of pathogenic variants of these genes is characterized by pronounced ethnic and population specificity, including the presence of founder mutations. Data on the spectrum of germline BRCA1/BRCA2 variants in the Kazakh population remain limited, which hinders their application in clinical practice and genetic counseling.

Objective: To study the spectrum of germline mutations in the BRCA1 and BRCA2 genes in patients with breast cancer and women with a family history in the Kazakh population and to identify the founder mutation.

Materials and Methods: The study included 544 women of Kazakh ethnicity with breast cancer or a family history of cancer. DNA was isolated from peripheral blood lymphocytes according to the manufacturer's protocol. Exons and adjacent intronic regions of the BRCA1 and BRCA2 genes were sequenced by NGS. Variants were classified by clinical significance, and their spectrum and distribution by gene, type, and localization were analyzed.

Results: Of the 544 examined patients, 178 (32.7%) were found to have mutations in the BRCA genes. Mutations in the BRCA1 gene were detected in 35 patients (19.7%), in the BRCA2 gene — in 119 patients (66.8%), and mutations in both genes — in 24 patients (13.5%).

The study identified a total of 125 BRCA gene variants. Sequence analysis revealed 37 pathogenic variants in 81 patients, 83 likely pathogenic variants in 104 patients, 1 likely benign variant in 6 patients, 2 benign variants in 6 patients, and 2 variants of uncertain clinical significance in 2 patients.

Among BRCA1 gene variants, the most common was a deletion of exon 6, detected in 11 patients (6.1%). Deletions of exons 2, 13, and 20 were found in 7 patients each (3.9%), while deletions of exons 8 and 23, as well as variants BRCA1 c.3214delC and BRCA1 c.1044_1045insC, were found in 3 patients each (1.7%).

Among the identified BRCA2 gene variants, the most common was a deletion of exon 16, detected in 37 patients. The variant c.24_27delGCCAinsCG was identified in 15 patients, c.2600_2601insA in 12 patients, and c.9241_9242insA in 11 patients.

Conclusions: The spectrum of germline BRCA1/BRCA2 mutations in the Kazakh population is characterized by a predominance of BRCA2 gene variants. Deletion of exon 16 of the BRCA2 gene was identified as a founder mutation.

Keywords: BRCA1, BRCA2, Breast Cancer, Sequencing, Germline Mutation