عنوان مقاله:

Novel BRCA1 and BRCA2 Deleterious Mutations and Unclassified Variants in Egyptian Female Breast Cancer Patients

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خلاصه مقاله:

Introduction: Breast cancer is the most common malignancy among females worldwide and the leading cause of cancer death in economically developing countries. The world s oldest documented cancer case hails from Ancient Egypt 3500 years BC and the Egyptian population shows high-degree of genetic diversity due to its complex ethnic origins. The contribution of BRCA1/BRCA2 mutations to the burden of breast cancer in Egypt has not been extensively evaluated. Methods: A series of 103 Egyptian female breast cancer patients, unselected for age of onset or family history, were included in the study. Mutational screening of exons 2 and 20 of BRCA1 and exons 9 and 11 of BRCA2 genes was performed using HRM analysis followed by direct sequencing of detected variants. The potential clinical effect of the novel missense mutations on protein structure and function was evaluated using In Silico prediction tools. Results: Deleterious mutations were observed in 29 (28.15%) cases. Of those, 13 (44.8%) carried BRCA1 mutations, 13 (44.8%) carried BRCA2 mutations and 3 (10.34%) carried both BRCA1 and BRCA2 mutations. Thirteen carriers (44.8%) reported positive family history of breast cancer, 14 (48.27%) had early onset and 5 cases had bilateral disease. Twenty different sequence variants were identified: 5 novel frame shift mutations; 1 in BRCA1 (c.5205delA) and 4 in BRCA2 (c.3641delT, c.3291dupT, c.3292delA, and c.787dupA), 1 novel nonsense mutation (BRCA2 c.3280A> T), 2 previously described missense mutations (BRCA1 c.117T> G and c.110C> A), 1 silent mutation (BRCA2 c.3396A> G) and 11 unclassified variants, 8 of which were novel. Novel mutations were submitted to NCBI Clinvar database. All the observed deleterious mutations were recurrent, except BRCA1 c.110C> A mutation which was detected once. The BRCA1 frame shift mutation c.5205delA was observed in high frequency (16/103, 15.5%) in our cohort. Unclassified variants were identified in 32 (31%) cases, 15 of them had a co-occurring deleterious mutation. Patients with BRCA mutations tended to have early onset breast cancer compared to non-carriers (P=0.002), more often premenopausal (P=0.006), with a familial history of breast cancer as well as other cancers (P=0.005).Conclusion: This study provides the results of our attempt to delineate the genetic aspect of breast cancer among the Egyptian population and emphasizes the necessity of implementing screening and preventive strategies as part of the national public health policy to facilitate early diagnosis and proper counseling for breast cancer patients in Egypt.

کلمات کلیدی:
.BRCA1;BRCA2;Breast Cancer;Egypt;HRM;Germline Mutations;Unclassified Variants