GERMLINE BRCA1 AND BRCA2 MUTATIONS IN HIGH-RISK PATIENTS IN MEDELLIN, COLOMBIA

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BACKGROUND: Germline mutations in BRCA1 and BRCA2 account for 30-50% of inherited breast cancers and 40% of ovarian cancers. Three founder mutations and a few sporadic mutations have been identified in Colombia. The pattern of mutations in different regions of the country remains largely unknown. This study describes the frequency and type of germline mutations in BRCA genes in patients undergoing genetic testing for Hereditary Breast and Ovarian Cancer syndrome (HBOC) in a Comprehensive Cancer Center in Medellín, Colombia.
METHODS: We enrolled 45 women referred to the Genetics Service of the Instituto de Cancerología Las Americas who were tested for HBOC or HBOC and other hereditary cancer syndromes according to NCCN 2015 guidelines. Full BRCA1/2 sequencing and detection of large rearrangements or multi-gene panel testing including BRCA1/2 were performed by Myriad (12 BRCA1/2 comprehensive tests and 33 myRisk panels).
RESULTS: Seven patients (15.5%) carried deleterious mutations (5 in BRCA1 and 2 in BRCA2). Among these, one was a novel mutation (BRCA2: c.9246dupG), two were not reported in Colombian women (BRCA1: c.213-12A>G, BRCA2 del exons 15-16), and none were previously described Colombian founder mutations. Six mutation-carriers had a history of breast cancer (median age of diagnosis of 35.3 years), one of ovarian cancer and five had family history of breast and/or ovarian and/or pancreatic cancer. No deleterious mutations were found in other genes and 14/33 (42.4%) multi-gene panels reported variants of unknown significance in other genes.
CONCLUSIONS: We found a novel BRCA2 mutation and two BRCA1/2 mutations not previously reported in Colombia. This suggests the necessity of performing full gene sequencing and large rearrangement testing of BRCA1/2 in our population, which currently is not widely done. We propose the creation of an open access Colombian database of genetic variants in high-penetrant cancer genes.