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1165 – Identification of a novel pathogenic germline variant in the BRCA2 gene in patients with hereditary breast and ovarian cancer syndrome

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Introduction: Hereditary breast and ovarian cancer (HBOC) syndrome is associated with pathogenic variants in the BRCA1 and BRCA2 genes, which are essential for DNA repair and the maintenance of genomic integrity. Thousands of variants have been described in BRCA2, with more than 5,000 classified as pathogenic in public databases. Alterations in this gene significantly increase the risk of neoplasms, especially breast cancer. The identification of novel germline variants is essential to improve molecular diagnosis, genetic counseling, and clinical management.

Methods: This observational study involved patients with clinical suspicion of HBOC treated at the Human Genetics Center of the Federal University of Goiás. Genomic DNA samples extracted from peripheral blood were analyzed. BRCA2 sequencing was performed using next-generation sequencing. Identified variants were analyzed using bioinformatics tools, compared with data from public databases (ClinVar and gnomAD), and classified according to the guidelines of the American College of Medical Genetics and Genomics (ACMG).

Results: A 48-year-old female patient diagnosed with invasive ductal breast carcinoma was referred for oncogenetic evaluation. The BRCA2 variant c.4245_4246insA was identified and classified as likely pathogenic. This alteration consists of an insertion with the potential to cause a frameshift, resulting in a truncated protein and probable loss of function. The variant was neither found in population databases nor previously described in the scientific literature, supporting its rare and possibly novel nature.

Conclusion: The identification of this novel germline variant reinforces the central role of BRCA2 in hereditary breast cancer predisposition and highlights the importance of genetic testing in individuals with clinical suspicion of HBOC. This finding contributes to the enrichment of genomic databases and to advances in oncogenetics, with further studies being needed for better functional and clinical characterization.

Ethics: Research Ethics Committee Approval (CAAE 50626315.6.3001.0031).

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Keywords: breast neoplasms; germ-line mutation; high-throughput nucleotide sequencing; genetic testing.