TÍTULO: HEREDITARY BREAST AND OVARIAN CANCER: WHEN A BRCA2 IS MISSING

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Resumo:
Introdução
Hereditary breast and ovarian cancer (HBOC) due to mutations in the BRCA1 and BRCA2 genes is the most common cause of hereditary forms of both breast and ovarian cancer. The majority of BRCA1 and BRCA2 mutations (≥80%) consist of single base changes or deletions/insertions of small numbers of bases that have significant impact on protein function. A minority of mutations in these genes are large rearrangements of DNA segments that disrupt gene function, consisting primarily of deletions and duplications of 1 or more exons.

Objetivos e Métodos
We report a 55yo female patient referred to our Medical Genetics Clinic due to personal and family history of breast cancer. At 53yo she was diagnosed with breast cancer and underwent tumorectomy of the left breast and sentinel lymph node biopsy. The histological diagnosis established an invasive carcinoma type luminal B with negative sentinel lymph node. From the family history to note: mother diagnosed with breast cancer at 57yo and maternal grandmother diagnosed with metastatic breast cancer at 67yo. Both died shortly after diagnosis.

Resultados
BRCA1 and BRCA2 gene panel concurrently with deletion/duplication analysis was performed and a heterozygous deletion of BRCA2 was detected and classified as a pathogenic variant. In order to clarify the extent of the BRCA2 deletion, microarray was performed and revealed a 13q13.1 microdeletion involving the BRCA2 gene.
At-risk relatives await study for detection of the familial variant on BRCA2.

Conclusões
Genomic rearrangements of the BRCA2 gene account for approximately 10% of the BRCA2 mutational spectrum. According to the data available in the literature this is the first case of HBOC due to deletion of the entire BRCA2 gene to be described in Portugal. The 13q13.1 deletion is not associated with other clinical features besides HBOC due to BRCA2 deletion, and the phenotype overlaps with HBOC cause by point mutations and smaller deletions/duplications. Once a BRCA2 mutation has been identified in a family, testing of at-risk relatives can identify those family members who also have the familial mutation and thus need increased surveillance/screening and primary prevention options should be suggested, including prophylactic surgery. With this in mind, it is appropriate to consider the routine inclusion of assays for the comprehensive detection of large rearrangements as part of routine testing for BRCA1 and BRCA2 for all patients at risk for HBOC.

Palavras Chave: BRCA2; Breast Cancer; Microdeletion