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DELETERIOUS VARIANTS IN RAD51C GENE AND BREAST CANCER – REPORT OF THREE PATIENTS WITH TRIPLE-NEGATIVE BREAST CANCER

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RAD51C is a gene associated with hereditary predisposition to ovarian cancer, and its association with hereditary breast cancer was controversial for a while. Current evidence demonstrates that RAD51C deleterious variants increase the risk of estrogen receptor-negative breast cancer. This study presents three unrelated patients with triple-negative breast tumors with heterozygous deleterious RAD51C variants. The first patient was diagnosed with post-menopausal breast cancer at 55 years of age and treated with conservative surgery and adjuvant chemotherapy. Her sister had breast cancer at 49 years of age. Multigene panel showed a heterozygous pathogenic variant in RAD51C:c.93del; p.(Phe32Serfs*8). The second patient was diagnosed at 48 years of age and treated with neoadjuvant chemotherapy, followed by a conservative surgery with lymph node dissection and radiotherapy. Her sister had triple-negative breast cancer at 64 years of age; her maternal cousin had breast cancer at 58 years of age. Multigene panel disclosed a heterozygous pathogenic variant in RAD51C:c.404G>A; p.(Cys135Tyr). The third patient, detected with the same mutation, was diagnosed with triple-negative breast cancer at 39 years of age and treated with neoadjuvant chemotherapy, bilateral mastectomy, and adjuvant radiotherapy. Her paternal aunt had ovarian cancer, her paternal grandfather had prostate cancer, and her sister had breast cancer at 40 years of age. Genetic counseling was provided for all patients, along with the recommendation of risk-reducing salpingo-oophorectomy, due to ovarian cancer risk. This study adds evidence for the inclusion of the RAD51C gene in multigene panels as a relevant gene to be screened in patients with triple-negative breast cancer.

**All three patients signed an informed consent.

Keywords: Triple-negative breast cancer. Hereditary cancer predisposition.