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1029 – Simultaneous BRCA1 and PALB2 pathogenic variants in a patient with triple-negative breast cancer

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Introduction: Triple-negative breast cancer (TNBC) accounts for approximately 15% of breast cancers. BRCA1 mutations occur in up to 20% of TNBC cases; simultaneous pathogenic variants in BRCA1 and PALB2 in a single patient are exceedingly rare, with poorly characterized combined clinical implications.

Case report: A 54-year-old woman presented in 2017 with a progressively enlarging right breast mass. Physical examination revealed a 6 × 5 cm tumor; mammography showed a 4 cm irregular nodule and ultrasonography measured a 5 cm lesion, with no axillary lymphadenopathy. Personal history included bariatric surgery in 2015. Family history was notable for paternal lymphoma, maternal bladder cancer (two diagnoses), maternal aunt with gastric cancer, paternal grandfather with bone cancer, and maternal cousin with colorectal cancer. Core biopsy confirmed invasive breast carcinoma, no special type, grade 3, triple-negative, with Ki-67 expression of 80%, staged as T3N0M0. Staging computed tomography and bone scintigraphy showed no metastases. Neoadjuvant chemotherapy with doxorubicin, carboplatin, and paclitaxel achieved complete clinical and radiological response. Segmental resection with sentinel lymph node biopsy followed by radiotherapy confirmed complete pathological response with three negative sentinel nodes. Multigene panel testing (16 genes) identified two simultaneous pathogenic variants: BRCA1 (p.Gln1111Asnfs*5) and PALB2 (p.Gln348*). The patient is currently under investigation for a suspected ovarian malignancy (carbohydrate antigen 125 [CA-125] 450 U/mL).

Discussion: The co-occurrence of pathogenic variants in BRCA1 and PALB2 in a single patient is exceedingly rare. PALB2 mutations confer a lifetime breast cancer risk of 35–60%; their interaction with concurrent BRCA1 mutations is not well characterized. Complete pathological response to platinum-based chemotherapy is consistent with BRCA1-related homologous recombination deficiency. The suspected ovarian malignancy raises concern for a secondary BRCA1-associated tumor. This case supports multigene panel testing in TNBC, which is capable of detecting co-occurring actionable variants with implications for treatment, surveillance, and cascade testing for at-risk relatives.

Ethics: Research Ethics Committee Approval (CAAE 30154720.0.0000.5209).

Keywords: breast neoplasms; triple-negative breast neoplasms; mutation.