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CASE REPORT

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Metachronous breast cancer in a *BRCA1* mutation carrier

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ABSTRACT

Breast cancer is the most common neoplasm among women in Poland and worldwide. Approximately 8000 women die from breast cancer in Poland each year. It is the second leading cause of cancer-related deaths among Polish women, following lung cancer. This cancer is highly heterogeneous in terms of morphology as well as molecular characteristics, and it requires different therapeutic approaches. Several risk factors for breast cancer have been identified, including genetic, environmental, and individual factors. Mutations in the *BRCA1* and *BRCA2* genes are the best-known genetic factors responsible for approximately 5–10% of breast cancer cases worldwide. The risk of developing bilateral breast cancer in patients with *BRCA1* mutation is significantly higher than in the general population. Furthermore, attention is drawn to the increased risk of metachronous tumors in patients with a *BRCA1* gene mutation who have previously had breast cancer. This article presents a case report on a patient with metachronous breast cancer who has developed bone and liver metastases. Based on the genetic test result showing a *BRCA1* mutation, the patient was qualified for talazoparib treatment.

Keywords: breast cancer, metachronous tumors, *BRCA1* mutation

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Introduction

Breast cancer is the most common malignant tumor among women, and one of the three most prevalent cancers worldwide alongside lung cancer and colorectal cancer [1]. It is estimated that approximately 1.6 million new cases of breast cancer occur worldwide each year, and its incidence continues to increase [2]. In 2020, about 17500 new cases of breast cancer were diagnosed in Poland, and nearly 8 000 patients died of this disease. The highest incidence is observed among women aged 55–65, and the highest number of deaths was recorded in the sixth and seventh decades of life [3]. Mortality from breast cancer may decrease due to early diagnosis, disease detection, and the development of new treatment methods. However, breast cancer remains the leading cause of cancer-related deaths among women in developing countries and the second most common cause of death — after lung cancer — in developed countries [1]. Most breast cancers are invasive tumors that spread to surrounding tissues and lymph nodes. Currently, there are 21 histologically different types of breast cancer and 4 different molecular subtypes [4]. The vast majority of breast cancers are sporadic tumors (approximately 90%), that develop due to somatic mutations in an individual's lifetime [2]. Many known factors may contribute to the development of breast cancer including genetic, hormonal, environmental, dietary, and reproductive factors as well as exposure to ionizing radiation [4]. About 5–10% of breast cancer cases occur in individuals with a known hereditary germline mutation. Among these genetic factors, mutations in the *BRCA1* and *BRCA2* genes, responsible for DNA repair, have been best characterized. The risk of developing breast cancer in carriers of mutated genes is significantly higher than in the general population and ranges from 69% to 72%. There is also a significantly higher risk of developing bilateral breast cancer in this population [5]. Additionally, these individuals are at an increased risk of developing ovarian, pancreatic, and prostate cancer [2].

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Metachronous tumors occurring in *BRCA1* mutation carriers who have previously had breast cancer are more common than in non-carriers, with second breast cancer being most frequently observed [5].

Case report

The patient, aged 35, was diagnosed with left breast cancer (triple-negative subtype, clinical stage pT1cN1) in 2010. The patient underwent breast-conserving surgery and received 6 cycles of adjuvant chemotherapy with doxorubicin and cyclophosphamide as well as adjuvant radiotherapy. In 2021, suspicion of metachronous right breast cancer was raised. Biopsy showed invasive ductal carcinoma grade 3 and luminal B subtype. Immunohistochemical analysis of the tumor cells showed estrogen receptor expression (10%), progesterone receptor expression (5%), negative HER2 status, and a Ki-67 index of 70%. The patient underwent surgery and postoperative examination showed stage pT1cN0. Despite being informed about the risks associated with her decision, the patient declined adjuvant chemotherapy as well as hormonal therapy in the form of goserelin and zoledronic acid. The patient was still menstruating, which is why zoledronic acid was suggested only on the condition of obtaining her consent to goserelin therapy to pharmacologically induce menopause. Treatment with tamoxifen was initiated (as the only form of systemic therapy acceptable for the patient) along with adjuvant radiotherapy.

In May 2022 abdominal computed tomography (CT) raised suspicion of a secondary lesion in the liver. Metastatic disease was confirmed in June on positron emission tomography (PET), which showed skeletal and liver secondary deposits. After a multidisciplinary consultation, a liver biopsy was performed to determine metastasis phenotype. Zoledronic acid therapy was initiated and — after an oncological consultation on radiation – the patient underwent palliative radiotherapy for the Th3–Th5 segment of the spine as well as the left iliac crest and sacrum. The pathology result of the liver biopsy was inconclusive, as only benign tissue was obtained.

Due to the patient's rapidly deteriorating general condition, low expression of steroid receptors in the primary tumor, and impending visceral crisis, palliative chemotherapy with paclitaxel (80 mg/m^2 every week) was initiated, which was completed in October.

In September 2022, remission of liver lesions was observed. A liver biopsy was repeated, and it indicated metastasis of adenocarcinoma. Immunohistochemical analysis of the tumor cells demonstrated the absence of estrogen receptors (ER–), progesterone receptors (PR–) and HER2(–). In January 2023 disease progression was observed, confirming the metastasis of "triple-negative" breast cancer with disease progression after the first-line palliative chemotherapy (paclitaxel). Genetic testing identified the presence of a *BRCA1* mutation (5382 ins. C). Based on this, the patient received talazoparib. After three months of therapy, partial remission (PR) was found according to RECIST 1.1 criteria. The patient continues the treatment.

Discussion

The risk of breast cancer is higher in women with a history of breast cancer and ranges from 10–15% for a 55-year-old woman with a previous breast cancer compared to 2.5% for a healthy 55-year-old woman during a 15-year observation period. From the initial diagnosis, the risk of developing metachronous breast cancer significantly increases over time [5]. The prevalence of *BRCA1* gene mutations in the Polish population is approximately 6% in breast cancer patients diagnosed before the age of 50 [6]. Breast cancers associated with *BRCA1* mutation occur at an early age (42–45 years) and are bilateral in 18–32% of cases [6–9]. The presence of a *BRCA1* mutation increases the risk of developing breast cancer to 50–80% and ovarian cancer to approximately 40%, depending on the type of mutation [10, 11]. In a study by Kruczała et al. [5], the development of metachronous malignancy was observed in 50% of patients with *BRCA1* mutation, with 38% of cases being second breast cancer compared to only 4.8% with metachronous ovarian cancer (possibly because 40% of patients in the studied population underwent prophylactic hysterectomy with bilateral adnexectomy). Due to the high incidence of breast cancer and a significant number of patients undergoing radical treatment as well as the increasingly common and accessible diagnostics for *BRCA1* gene mutations, it is expected that the number of cancer patients with identified mutations will increase in daily clinical practice. With this in mind, it is necessary to raise awareness of the scale of metachronous tumors in patients with *BRCA1* mutations in the medical community, intensify surveillance of *BRCA1* mutation carriers after breast cancer treatment to detect the occurrence of subsequent tumors and consider prophylactic bilateral adnexectomy and mastectomy for *BRCA1* mutation carriers previously treated for breast cancer [5].

A significant prognostic factor in breast cancer patients is the presence of expression of ER and PR as well as HER2 on tumor cells. This is particularly important in the case of tumor metastases, as their presence is one of the most common causes of treatment failure in oncology. The expression status of ER, PR, and HER2 on metastatic tumor cancer cells is crucial for selecting

a therapeutic strategy. However, it should be noted that there is often a significant discordance in the expression of ER and PR receptors between metastatic tumors and the primary tumor focus, while the expression status of HER2 remains relatively stable [12]. In the case of the described patient, the biopsy of liver metastases revealed a discrepancy in the expression of ER and PR receptors compared to the metachronous cancer that occurred later. This suggests the presence of "triple-negative" breast cancer metastases which occurred in the patient in 2010.

Article Information and Declarations

Ethics statement

The patient's consent was obtained for the presentation of a clinical case.

Author contributions

K.P.: responsible for conception, design, execution, writing the paper; I.R.: responsible for conception, design, execution, writing the paper; M.K.: responsible for conception, design, execution, writing the paper. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare no conflict of interest.

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Supplementary material

None.

References

1. Harbeck N, Gnant M. Breast cancer. Lancet. 2017; 389(10074): 1134–1150, doi: 10.1016/S0140-6736(16)31891-8, indexed in Pubmed: 27865536.
2. Thorat MA, Balasubramanian R. Breast cancer prevention in high-risk women. Best Pract Res Clin Obstet Gynaecol. 2020; 65: 18–31, doi: 10.1016/j.bpobgyn.2019.11.006, indexed in Pubmed: 31862315.
3. Wojciechowska U, Barańska K, Michałek I. Nowotwory Złośliwe w Polsce w 2020 roku. Krajowy Rejestr Nowotworów Narodowy Instytut Onkologii, Warszawa 2020.
4. Winters S, Martin C, Murphy D, et al. Breast Cancer Epidemiology, Prevention, and Screening. Prog Mol Biol Transl Sci. 2017; 151: 1–32, doi: 10.1016/bs.pmbts.2017.07.002, indexed in Pubmed: 29096890.
5. Kruczała M, Jasiówka M, Marczyk E, et al. Metachronic cancers among women with breast cancer and BRCA1 mutation. Oncol Clin Pract. 2017; 13(6): 264–267, doi: 10.5603/OCP.2017.0039.
6. Lubiński J, Górski B, Huzarski T, et al. BRCA1-positive breast cancers in young women from Poland. Breast Cancer Res Treat. 2006; 99(1): 71–76, doi: 10.1007/s10549-006-9182-3, indexed in Pubmed: 16541315.
7. Marcus JN, Watson P, Page DL, et al. Hereditary breast cancer: pathobiology, prognosis, and BRCA1 and BRCA2 gene linkage. Cancer. 1996; 77(4): 697–709, doi: 10.1002/(sici)1097-0142(19960215)77:4<697::aid-cncr16>3.0.co;2-w, indexed in Pubmed: 8616762.
8. Martin AM, Blackwood MA, Antin-Ozerkis D, et al. Germline mutations in BRCA1 and BRCA2 in breast-ovarian families from a breast cancer risk evaluation clinic. J Clin Oncol. 2001; 19(8): 2247–2253, doi: 10.1200/JCO.2001.19.8.2247, indexed in Pubmed: 11304778.
9. Loman N, Johannsson O, Bendahl P, et al. Prognosis and clinical presentation of BRCA2-associated breast cancer. Eur J Cancer. 2000; 36(11): 1365–1373, doi: 10.1016/s0959-8049(00)00098-8, indexed in Pubmed: 10899649.
10. Antoniou AC, Pharoah PDP, Narod S, et al. Breast and ovarian cancer risks to carriers of the BRCA1 5382insC and 185delAG and BRCA2 6174delT mutations: a combined analysis of 22 population based studies. J Med Genet. 2005; 42(7): 602–603, doi: 10.1136/jmg.2004.024133, indexed in Pubmed: 15994883.
11. Gronwald J, Huzarski T, Byrski B, et al. Cancer risks in first degree relatives of BRCA1 mutation carriers: effects of mutation and proband disease status. J Med Genet. 2006; 43(5): 424–428, doi: 10.1136/jmg.2005.036921, indexed in Pubmed: 16227521.
12. Qu Q, Zong Yu, Fei Xc, et al. The importance of biopsy in clinically diagnosed metastatic lesions in patients with breast cancer. World J Surg Oncol. 2014; 12: 93, doi: 10.1186/1477-7819-12-93, indexed in Pubmed: 24721777.