e-ISSN 2414-1518

Galician Medical Journal

Scientific and Practical Journal of
Ivano-Frankivsk National Medical University

I.B. Diakiv

Ethiopathogenetic Factors of Precancerous Gynecological Diseases in Patients with Breast Cancer

Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine

Keywords: ***breast cancer, precancerous gynecological disease, heredity, prevention***

Abstract.

The objective of the research was to assess risk factors for precancerous gynecological disease (PGD) in patients with breast cancer (BC) after comprehensive and combination treatment.

Materials and methods. The study was based on the results of examination and treatment of 40 patients suffering from BC with PGD which developed at different times after treatment. In patients with breast cancer PGD included precancerous uterine body disease in 26 (65.0 %) patients, the precancerous ovariopathies in 9 (22.5 %) individuals and precancerous cervical disease in 5 (12.5%) cases.

Results of the research. Precancerous uterine body disease occurred most often in most patients with BC after treatment. It included atypical endometrial hyperplasia in 19 (73.0%) patients and proliferating nodular leiomyoma of uterine body in 7 (27.0%) cases. Precancerous ovariopathies detected in patients with BC included allied papillary mucinous cystadenoma of ovaries in 6 (66.7%) patients and endometrioid cystadenoma in 3 (33.3%) cases. Precancerous cervical disease detected in patients with BC included severe cervical intraepithelial neoplasia (CIN III). CIN III was found in 5 (12.5%) cases.

Conclusions. According to the results of the analysis and literature data, PGD occurred in patients with BC. The results indicated that hormonal factors, burdened oncology case history and results of immunohistochemical and molecular genetic diagnosis of breast tumors are important in PGD development in patients with BC.

Copyright © Author(s), 2016

Problem statement and analysis of the recent research

Breast cancer (BC) takes the lead in the structure of cancer incidence and mortality of the female population of Ukraine and most economically developed countries. According to National Cancer Registry, the incidence of breast cancer in Ukraine in 2013 constituted 72.3 per 100 thousand and mortality amounted 31.6 per 100 thousand female population. 37% of patients with breast cancer are women of reproductive and working age [1]. 5-year survival index of breast cancer in Ukraine (2013) was 53.8% while it constituted 75-80 % in Western Europe countries and 85-92% in the USA [1, 2].

Breast cancer refers to hormone-related and hormone dependent tumors as well as ovarian tumor and tumor of uterus. Latent or distinct chronic hyperestrogenemia is the main common factor for all the above mentioned tumors except metabolic factors [3, 4]. This indicates that breast cancer is a systemic disease [5, 6].

Cases of precancerous gynecological diseases (PGD) in patients with breast cancer have been increasingly detected over the last decades. The absence of downward trend in the incidence of reproductive system diseases in women justifies the increased attention to this problem. New programs aimed at prevention and early diagnosis of cancer tumors including ovarian tumor and tumor of uterus in patients with breast cancer are required for the solution of the problem. PGD development belongs to poorly studied diseases although the interest in them appeared in the 1970s. Scientific research on PGD clinical features and course was presented in a number of monographs and articles [7, 8].

Results of the clinical studies indicate the increase in PGD incidence in the recent years which can be explained by several factors. First of all, this may occur due to the optimization of tumor diagnostics by introduction of new methods of patients' examination (endoscopy and ultrasonic diagnosis, computed tomography and magnetic resonance imaging, immunoenzymometric, immunomorphologic and molecular genetic methods of surgical specimen research). In addition, PGD development in patients with BC is possible after treatment of cancer patients, especially young patients, using chemotherapy and radiotherapy which are characterized by mutagenic effect on cells. Harmful environmental factors, working conditions, immunodeficiency, and lifestyle are also a precondition for the development of this disease [9, 10].

However, despite the long-time studies, their comprehensive clinical characterization is still absent due to the variety of histological types, principles of their prevention have not been developed yet, approaches to patients' monitoring have not been determined, risk groups concerning PGD development after treatment of patients with breast cancer have not been selected.

The objective of the research was to assess risk factors for precancerous gynecological disease in patients with breast cancer after comprehensive and combination treatment.

Materials and methods of the research

The study was based on the results of examination and treatment of 40 patients suffering from BC with PGD which developed at different times after treatment. All the patients were treated at Ivano-Frankivsk Regional Clinical Oncology Center from 1996 to 2015.

The age of patients with BC involved into the studies ranged from 31 to 76 years, the average age was 47.3±1.7.

In patients suffering from BC with PGD BC stage II was detected in 18 (45.0 %) patients, BC stage I was observed in 11 (27.5 %) patients, BC stage III was found in 10 (25.0 %) individuals, BC stage IV was detected in 1 (2.5 %) patient.

According to the results of histologic examination of biopsy and surgical specimen infiltrating breast carcinoma was verified in 33 (82.5%) patients, intraductal noninfiltrating

carcinoma was detected in 3 (7.5 %) cases and mucinous carcinoma was observed in 2 (5.0 %) patients.

In all these patients with breast cancer PGD occurred including precancerous uterine body disease in 26 (65.0 %) patients, the precancerous ovariopathies in 9 (22.5 %) individuals and precancerous cervical disease in 5 (12.5%) cases.

Variational and statistical analysis was applied to assess the reliability of the results using a personal computer and such applications as Microsoft® Office Excel® 2007 and Statistica v.6.1 (Statsoft Inc., USA). The database was formed on the basis of Ms Excel tables.

Results of the research and their discussion

Precancerous uterine body disease (PUBD) occurred most often in most patients with BC after treatment. PUBD in patients with BC was detected in 26 (65.0 %). PUBD in patients with BC included atypical endometrial hyperplasia and proliferating nodular leiomyoma of uterine body. Atypical endometrial hyperplasia was detected more often, namely in 19 (73.0%) patients and proliferating nodular leiomyoma of uterine body was diagnosed in 7 (27.0%) cases.

Patients' age ranged between 38 and 77 years at the time of PUBD onset.

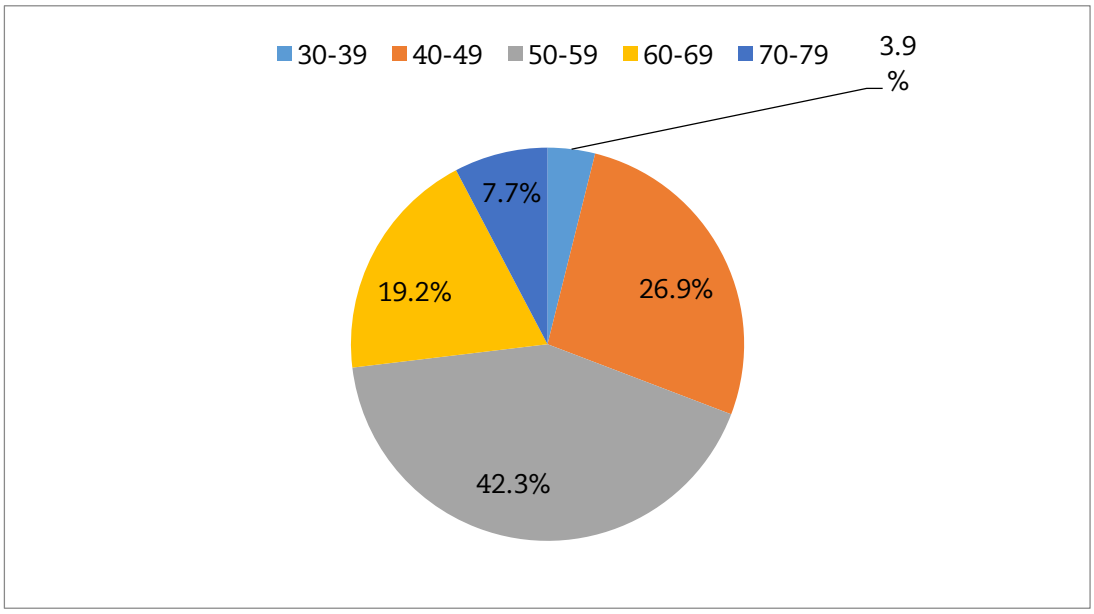

Fig 1. Distribution of patients who experienced PUBD after breast cancer treatment by age groups

The largest number of patients with PUBD was observed in the age group of 50-59 years, namely 11 (42.3%) patients. The age group of 30-39 years included 1 (3.9 %) patient. The age group of 40-49 years consisted of 7 (26.9 %) patients. Older age groups of 60-69 years and 70-79 years included 5 (19.2%) and 2 (7.7%) patients respectively.

Burdened oncology case history was detected in 14 (57 %) patients with PUBD. Two pregnancies occurred 10 (38.5 %) patients with PUBD, one pregnancy occurred in 7 (26.9 %) women, 3 and more pregnancies occurred in 8 (30.7 %) patients with PUBD. 1 (3.9%) patient was with primary infertility.

Analyzing menopause onset in women with PUBD premature menopause (before the age of 45) was detected in 8 (30.8 %) patients and late menopause (after the age of 55) was observed in 4 (15.4%) women. Natural menopause occurred in 14 (53.8 %) cases.

Immunohistochemical tumor status was also determined. Luminal A type (ER+ and/or RP+, HER2neu-) was determined in 15 (57.7 %) cases; luminal B type (ER+ and/or RP+, HER2 neu+) was

detected in 5 (19.2 %) patients; triple negative one (ER-, RP-, HER2neu-) was found in 2 (7.7 %) women.

Concomitant diseases diagnosed in patients with PUBD included cardio-vascular diseases in 21 (80.8 %) cases, endocrine diseases in 13 (50.0 %) patients, namely diabetes mellitus in 7 (53.8 %) patients and nodular goiter in 6 (46.2 %) patients. Overweight was detected in 12 (46.2 %) cases.

Surgical treatment, namely oophorohysterectomy type I, was conducted to all patients with PUBD.

Proliferating nodular leiomyoma of uterine body was diagnosed in 8 months after the end of BC treatment when rapid growth of the uterine body tumor was observed. Atypical endometrial hyperplasia occurred in 23 months.

Precancerous ovariopathies rank second after PUBD among gynecological pathology. Allied papillary mucinous cystadenoma of ovaries and endometrioid cystadenoma were detected in patients with precancerous ovariopathies. Precancerous ovariopathies were found in 9 (22.5 %) patients. Allied papillary mucinous cystadenoma of ovaries was diagnosed in 6 (66.7 %) cases and endometrioid cystadenoma was detected in 3 (33.3 %) women.

The average age of patient with precancerous ovariopathies ranged from 32 to 80 years.

3 (33.3 %) and 4 (44.5 %) patients with precancerous ovariopathies were observed in the age groups of 30-39 years and 40-49 years respectively. One patient was observed in the age group of 50-59 years and one in the age group of 80-89 years.

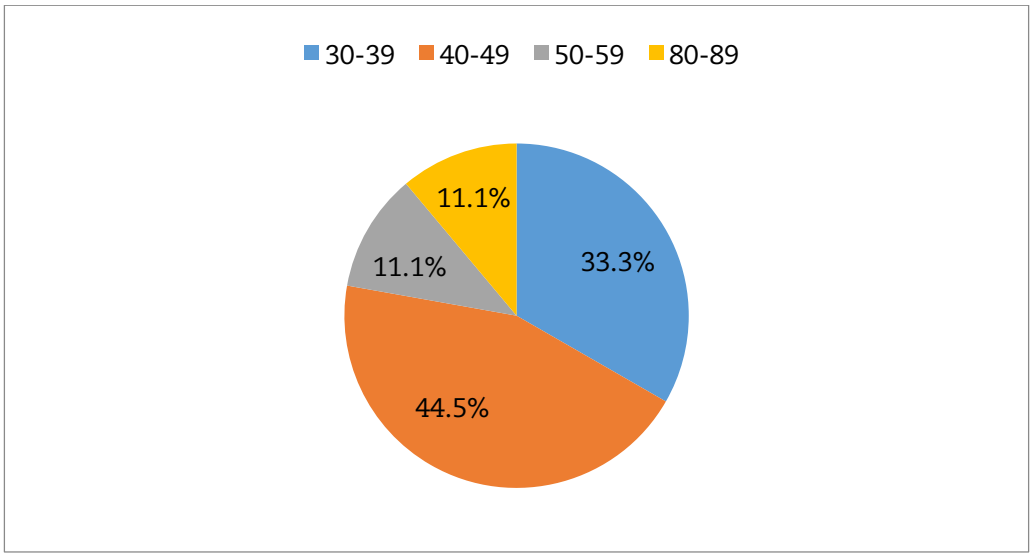

Fig 2. Distribution of patients who experienced precancerous ovariopathies after breast cancer treatment by age groups

Burdened oncology case history was detected in 7 (77.8 %) patients with precancerous ovariopathies. Thus, burdened oncology case history was a factor of precancerous ovariopathies development in patients with BC. 3 and more pregnancies occurred in 5 (55.6 %) patients with precancerous ovariopathies. Primary infertility was detected in 2 (22.2%) women.

Depending on menopause onset time premature menopause was detected in 5 (55.6 %) cases and late and natural menopause occurred in 2 (22.2 %) patients respectively.

The most common concomitant diseases included cardiovascular disease in 8 (88.9 %) patients, metabolic syndrome in 6 (66.7 %) cases and gastrointestinal diseases in 4 (44.4 %) women.

Cancer-specific marker CA-125 was determined in all patients with precancerous ovariopathies. CA-125 index was above normal level in 3 (33.3 %) patients, mean value constituted 32.55 IU/ml, maximum value amounted 157.1 IU/ml.

According to immunohistochemical and molecular genetic classification of tumor types, basal type was detected in 5 (55.6 %) patients with precancerous ovariopathies, luminal type A was observed in 1 (11.1%) patient and triple negative type was detected in 1 patient as well (11.1%).

Surgical treatment was performed to all patients with precancerous ovariopathies. Bilateral adnexectomy was performed in 4 (44.4 %) cases. 5 (55.6%) patients underwent oophorohysterectomy with omentum resection.

Precancerous ovariopathies occurred in all patients in about the same time, namely in 68 months, after the end of BC treatment.

According to precancerous ovariopathies analysis in patients with BC such factors as burdened oncology case history, primary infertility, and premature menopause were detected. Determining the receptor status of breast tumors in patients with precancerous ovariopathies, basal type was detected. Its prognosis for treatment is negative.

We analyzed the onset of precancerous cervical disease (PCD) after BC treatment. Precancerous cervical disease detected in patients with BC included severe cervical intraepithelial neoplasia (CIN III) in 5 (12.5%) cases.

The age of patients with PCD ranged from 36 to 48 years. The age group of 30-39 years included 2 (40 %) patients with PCD and the age group of 40-49 years consisted of 3 (60 %) women.

Cervical diathermic electro-conization with the following cryolysis was conducted to patients with CIN III. CIN III occurred in 50 months after the end of BC treatment.

Thus, taking into account the incidence of severe cervical intraepithelial neoplasia in patients with BC, regular cervical cytological examination during periodic health examination of the patient concerning BC was shown.

Conclusions

According to the results of the analysis and literature data patients with BC are at high risk of PGD development. The obtained results indicated that hormonal factors (primary infertility, or 3 and more pregnancies, violation of early menopause onset, concomitant endocrine diseases), burdened oncology case history and results of immunohistochemical and molecular genetic diagnosis of breast tumors (luminal type A, basal type) are important in PGD development in patients with BC. Therefore, there is a need for better detalization of clinical anamnestic data when examining patients with breast cancer and a comparison of clinical, endocrinologic, clinical and genealogical and pathological features of breast cancer and PGD. This can become the basis for PGD risk calculations.

Prospects for further research

Creating risk factors programs aimed at prevention and early detection of precancerous gynecologic neoplasms in patients with breast cancer will prevent the development of metachronous malignant tumors.

References

1. Shchepotin IB, Fedorenko ZP. Cancer in Ukraine, 2013–2014. Morbidity, mortality, performance of oncology service. Biulleten Nats. Kantser-reiestru Ukrainy. 2014; 14: 55–56.
2. Smolanka II, Skliar SYu. The modern view on the problem of diagnosis and treatment of breast cancer. Zhinochyi likar. 2008; 5: 8.
3. Bilynskyi BT, Shparyk YaV. Problems of drug treatment of breast cancer. Posibnyk dlia likariv. 2001; 160.
4. Semiglazov VF, Dilman VM. The role of receptors for estrogen and progesterone in hormonal therapy appointment for patients with breast cancer in different age groups. Prakticheskaya onkologiya. 2008; 2: 26-30.

5. Shchepotin IB, Zotov OS, Enhel OT. Primary multiple malignant tumors of the female reproductive system. Onkologiya. 2009; 11(4): 249-253.
6. Miller W, Santen R. Breast cancer screening compliance among young women in a free access healthcare system. J. Surg. Oncol. 2008; 97: 20-24.
7. Maksimov SYa. Primary multiple tumors of the female reproductive system. Prakticheskaya onkologiya. 2009; 10(2): 117–123.
8. Caldarella A, Crocetti E, Taddei GL, Paci E. Coexisting endometrial and ovarian carcinomas: a retrospective clinicopathological study.. Pathol Res Pract 2008 May;204(9):643-648. Available from: https://www.nlm.nih.gov/medlineplus/ovariancancer.html PubMed PMID: 18472354. doi: 10.1016/j.prp.2008.02.001.
9. Meindl A, Ditsch N, Kast K, Rhiem K, Schmutzler RK. Hereditary breast and ovarian cancer: new genes, new treatments, new concepts.. Dtsch Arztebl Int 2011 May;108(19):323-330. Available from: http://dx.doi.org/10.3238/arztebl.2011.0323 PubMed PMID: 21637635. doi: 10.3238/arztebl.2011.0323.
10. Popova TN, Selezneva TD, Barsukov VYu, Federov VYe. Peculiarities of the course and the difficulties of the diagnosis of multiple malignant neoplasms. Med. Almanakh. 2011; 2: 157–160.