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Metachronic Oncogynecological Tumors in Patients with Breast Cancer

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Abstract

Breast cancer (BC) is the most common form of cancer pathology in women. Over the past decade, more and more cases metachronic BC are detected. One of more frequent metachronic malignant tumors after treatment of BC are uterine cancer (UC) and ovarian cancer (OC). Metachronic malignant tumors belong to a little-studied cancer. Lack downward trend in the incidence of cancer of the female reproductive system justifies increased attention to this problem. For its solution requires new programs, aimed at the prevention and early diagnosis of malignant tumors, including metachronic UC and OC in patients with BC.

Keywords: breast cancer, metachronic cancer, precancer disease, prevention

Introduction

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. In the world each year more than 1 million of new cases of breast cancer are registered. Every year in the world are died 600 000 women from BC. The highest incidence of breast cancer in the United States registered 103 cases per 100 000 population. The highest incidence rate in Western Europe registered in the Netherlands 91,6 per 100 thousand female population, and the lowest- in Latvia- 42,2. The lowest incidence of BC in Japan is registered in the Central Asian and African countries^[1, 2].

BC 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 metachronic BC (MBC) 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 metachronic tumors of BC are required for the solution of the problem. This problem belongs to poorly studied diseases although the interest in them appeared in the 1970s. Scientific research to clinical features and course of MBC was presented in a number of monographs and articles^[7, 8].

Results of the clinical studies indicate the increase in MBC 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, MBC development in patients 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 metachronic tumors development after treatment of patients with BC have not been selected.

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The Aim of the Research

To assess risk factors for metachronic tumors development of patients with BC after combine or complex treatment.

Materials and Methods

The study is based on examination and treatment of 85 patients with BC, which after treatment have another cancer or precancerous gynecological diseases. All the patients were treated at Ivano-Frankivsk Regional Clinical Oncology Center from 1995 to 2015. In 45 (52,9%) patients after BC treatment have arisen oncogynecological disease, and 40 (47%) patients - precancerous gynecological diseases (PGD).

The age of patients with BC involved into the studies ranged from 24 to 83 years, the average age was $54,6 \pm 2,3$.

Results and Discussion

The most common second cancers, which emerged in patients with BC was UC, which occurred at an average of $97 \pm 6,4$ months after the treatment of BC. The patients age at the time of UC ranged from 41 to 80 years and averaged age was $62,1 \pm 1,4$ years.

Most patients were in the age group of 60-69 years - 12 (40,0%) women and 50-59 years - 10 (33,3%). In the youngest age group of 40-49 years were found 4 (13,3%) patients, and in the age group of 80-89 years - 1 (3,3%) patients.

From comorbidities in patients with UC often observed cardiovascular disease (CVC) in 58,4% of cases, endocrine – 47,1% (diabetes – 28,4% and nodular goiter-18,7%), combined with excessive body weight – 35,6%. Family oncoanamnesis detected in 16 (53,3%) patients with UC. Early menopause (before 45 years) was in 7 (23,3%) patients, and late (after 55 years) - 8 (26,7%) patients.

UC stage I was diagnosed in 22 (73,3%) patients, II stage in 7 (23,3%) patients with stage III and 1 (3,3%) patients. All patients at UC conducted surgical treatment. Panhysterectomy type I performed in 20 (66,7%) patients with UC, panhysterectomy type II in 10 (33,3%) patients.

After $73 \pm 8,2$ months after treatment of BC, are originated OC. OC was found in 15 (17,6%) cases of patients with BC. The age of OC patients ranged from 40 to 77 years and averaged $42 \pm 1,8$ years.

In the age group 50-59 years was 6 (40,0%) of patients with OC, a group of 40-49 - 4 (26,7%) patients, and in the age group 60-69 years and 70-79 years was 2 (13,3%) and 3 (20,0%) patients, respectively.

Family oncoanamnesis in patients with OC was found in 9 (60,0%) cases. Early menopause was observed in 3 (20,0%) patients with OC, late - in 2 (13,3%). Among comorbidities often dominated by cardiovascular disease – 56,9% of cases, the metabolic syndrome – 17,8% and gastro-intestinal tract – 29,6

OC diagnosed at stage III - 9 (60,0%) patients, in stage II - 4 (26,7%) in stage I - 2 (13,3%) patients. Patients with OC conducted determination of tumor markers CA-125. In 10 (66,7%) patients with CA-125 index was higher than normal, and the average was $89,82 \pm 11,3$ IU/ml, and the maximum value was 2038 IU/ml.

All patients with OC are conducted surgery treatment. In 13 (88,7%) patients completed panhysterectomy with omentectomy. In 2 (13,3%) held bilateral adnexectomy with resection of omentum.

In 40 (47,0%) patients with BC came PGD, precancerous uterine disease (PUD) in 26 (65,0%) patients, the ovaries in 9 (22,5%), and cervix in 5 (12,5%) cases.

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 PUD onset. The largest number of patients with PUD 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.

Family oncoanamnesis was detected in 14 (57%) patients with PUD. Two pregnancies occurred 10 (38,5%) patients with PUD, one pregnancy occurred in 7 (26,9%) women, 3 and more pregnancies occurred in 8 (30,7%) patients with PUD. 1 (3,9%) patient was with primary infertility.

Concomitant diseases diagnosed in patients with PUD 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 panhysterectomy type I, was conducted to all patients with PUD.

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 ovarioopathies rank second after PUD among gynecological pathology. Allied papillary mucinous cystadenoma of ovaries and endometrioid cystadenoma were detected in patients with precancerous ovarioopathies. Precancerous ovarioopathies 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 ovarioopathies ranged from 32 to 80 years. 3 (33,3%) and 4 (44,5%) patients with precancerous ovarioopathies 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.

Family oncoanamnesis was detected in 7 (77,8%) patients with precancerous ovarioopathies. 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 ovarioopathies. 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.

Surgical treatment was performed to all patients with precancerous ovarioopathies. Bilateral adnexectomy was performed in 4 (44,4%) cases. 5 (55,6%) patients underwent panhysterectomy with omentum resection.

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

We analyzed the onset of precancerous cervical disease (PCD) after BC treatment. PCD 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 electrocoagulation 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.

Conclusion

In 45 (52, 9%) patients after breast cancer treatment have arisen oncogynecology disease, 30 (35,3%) - UC, 15 (17.4%) - OC; and 40 (47%) patients - PGD: PUC in 26 (65,0%) patients, the ovaries in 9 (22,5%), and cervix in 5 (12,5%) cases. The obtained results indicated that hormonal factors, family oncoanamnesis. 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 metachronic breast cancer. This can become the basis for metachronic tumors risk calculations.

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