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Case report/Opis przypadku

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Received: 09.12.2013

Accepted: 21.01.2014

Published: 27.03.2014

### STATISTIC STATYSTYKA

Word count Liczba słów 994

Tables Tabele 0

Figures Ryciny 0

References Piśmiennictwo 9

### Summary

Breast cancer is the most common malignancy in women. The terms gestational breast cancer (GBC) and pregnancy-associated breast cancer are given to breast cancer that occurs during pregnancy and up to one year after delivery. We report a case of a 32 year old woman diagnosed with breast cancer during pregnancy. She was diagnosed with ductal invasive ER(-), PR(-), HER2(+) breast cancer in clinical stage IIA. The patient received neoadjuvant chemotherapy (four courses of doxorubicin and cyclophosphamide every three weeks) and had a cesarean section in 36 weeks of pregnancy. The male infant was healthy. Then the patient underwent radical modified mastectomy. Subsequently she received adjuvant chemotherapy (twelve courses of weekly paclitaxel), radiotherapy and immunotherapy with trastuzumab (seventeen courses every three weeks). There were not any side effects of the treatment and in control imaging examination there were not any abnormalities. Chemotherapy can be safely administered to women during the second and third trimesters of pregnancy.

**Key words:** breast cancer, pregnancy, treatment

### Streszczenie

Rak piersi jest najczęstszym nowotworem u kobiet. Określenie „rak piersi związany z ciążą” odnosi się do choroby rozpoznanej w ciąży lub w ciągu roku od porodu. Przedstawiamy przypadek raka piersi zdiagnozowanego w ciąży u 32-letniej chorej. Rozpoznano u niej inwazyjnego raka przewodowego ER(-), PR(-), HER2(+) w stopniu zaawansowania klinicznego IIA. Pacjentka otrzymała chemioterapię neoadiuwantową (cztery kursy doksorubicyny z cyklofosfamidem co trzy tygodnie) i miała wykonane cięcie cesarskie w 36 tygodniu ciąży. Noworodek płci męskiej był zdrowy. Pacjentka przebyła zmodyfikowaną radykalną mastektomię, a następnie otrzymała chemioterapię uzupełniającą (dwanaście kursów paklitakselu co tydzień), radioterapię oraz immunoterapię – trastuzumab (siedemnaście podań co trzy tygodnie). Leczenie nie wiązało się z żadnymi działaniami niepożądanymi. W badaniach kontrolnych nie stwierdzono nieprawidłowości. Chemioterapia może być bezpiecznie stosowana u chorych w drugim i trzecim trymestrze ciąży.

**Słowa kluczowe:** rak piersi, ciąża, leczenie

## INTRODUCTION

Breast cancer is the most common malignancy in women and represents 23% of all malignancies. It is rare in women under 35 years of age [1]. The terms gestational breast cancer (GBC) and pregnancy-associated breast cancer are given to breast cancer that occurs during pregnancy and up to one year after delivery [2]. The research showed that during diagnostics of abnormalities in breast examination 1-2% of patients is pregnant and the prevalence of breast cancer is 1/3000 – 1/10000 pregnancies. GBC occurs more often in BRCA1 mutation carriers which is probably connected with younger age of these patients [3]. As maternal age at the time of pregnancy continues to increase and the incidence of breast cancer is raising, the incidence of pregnancy associated with breast cancer may be expected to increase [4].

Prophylaxis, diagnostics and treatment of breast cancer during pregnancy is difficult. Physiological changes in breasts during pregnancy cause problems with breast examining either palpable or imaging and the diagnosis may be delayed even several (median five) months [3]. Pregnancy complicates the management of breast cancer because the need for treatment has to be balanced against the potential risks to the fetus particularly in the case when the use of chemotherapy is proposed [5]. Adjuvant chemotherapy has a well-established role in improving survival in early breast cancer [6]. Delays or modification of adjuvant treatment to ensure the birth of a healthy infant could potentially compromise maternal survival [5].

We present a case of a 32-year old woman diagnosed with breast cancer during pregnancy.

## CASE REPORT

The patient came to Oncology Center in Bydgoszcz in April 2012, 27 weeks pregnant because of a painful 1,5 cm tumor in right breast found during self-examination in March 2012. She gave birth once before. Ultrasonography performed 02.04.2012 showed a hypoechogenic tumor in the right breast of irregular blurred outlines size 18x17x14 mm at the 7 o'clock position and above a similar lesion size 9x9x10 mm and at the 10 o'clock position there was a cluster of similar lesions total size 28x20x14 mm. In the lower part of right axilla there were two hypoechogenic lymph nodes size 14 i 13 mm. Physical examination showed a tumor sized 2,5 cm in the right breast with blurred outlines, movable and clavicular lymph nodes were not palpable.

Aspiration biopsy was performed 03.04.2012 and did not confirmed breast cancer. Mammotome biopsy was performed 16.04.2012. Histopathological test showed carcinoma ductale invasivum Elston Ellis G3. The patient was qualified to neoadjuvant chemotherapy, cesarean section in 35 week of pregnancy and then mastectomy.

She started chemotherapy 25.04.2012 and received three courses of AC chemotherapy (doxorubicin 110 mg iv, cyclophosphamide 1100 mg iv) every three weeks,

ended 08.06.2012. Cesarean section was performed 20.06.2012 in 36 weeks of pregnancy. The male infant was given 8 points in Apgar scale. The course of postpartum was normal. The fourth course of chemotherapy was administered 29.06.2013.

The physical examination after four courses of chemotherapy showed complete remission. The radical modified right mastectomy was performed 26.07.2012. The histopathological test showed: carcinoma invasivum mammae post chemiotherapiam, destructio cellularis post therapiam fere totalis, Ki-67 (+) 90%, estrogen receptor (ER) (-), progesteron receptor (PgR) (-), HER 2 Protein (3+), E-cadherin (+). In 26 breast specimens only in one there was found a microscopic cancer lesion. In the specimen there were 22 axillary lymph nodes, four metastatic. The pathological classification was ypT-micN2a. Since 16.08.2012 the patient received paclitaxel 146 mg iv weekly (twelve courses) and trastuzumab every three weeks (initial dose 576 mg, maintenance doses were 432 mg iv, seventeen courses). She also received radical radiotherapy for the right side of the chest wall and right axillary and supraclavicular lymph nodes to the total dose of 45 Gy/g in 20 fractions. The radiotherapy was performed from 11.2012 to 12.2012 with good tolerance. Adjuvant therapy was ended 22.08.2013. In control imaging examination in 10.2013 (abdominal ultrasonography, chest radiogram, mammography) there were not any abnormalities.

## DISCUSSION

Diagnostic and therapeutic process during pregnancy has to retain maximal protection for the fetus and keeping fertility for the mother. Pregnancy enhances development of malignant tumors first of all because increased immunological tolerance and decreased cellular resistance [7]. Breast cancer in young women is biologically much more aggressive than in older women that the prognosis in younger women is worse [8]. Breast cancer in pregnancy is usually diagnosed in more advanced stages what partly explains worse therapy results. Research showed that 56-90% women with GBC are diagnosed with metastatic lymph nodes what may be a result of increased lymph drainage in breasts of pregnant women which promotes regional lymph nodes metastases [9].

In early surgical stages the best method is surgery – radical mastectomy or breast conserving therapy with radiotherapy after the delivery [3, 7]. The safest time for surgery is after the end of first trimester [3]. Radiotherapy may be performed during pregnancy with appropriate fetus protection and with use of optimal radiation dose only if absolutely necessary.

Chemotherapy is considered to be safe for mother and fetus after the end of first trimester [5]. Administration of cytostatic drugs like anthracyclines, methotrexate, cyclophosphamide or 5-fluorouracil was not connected with the risk of fetal abnormalities although there are reported early complications (lower birth mass, pancytopenia, growth retardation) or late complications (gonadal

dysfunction, impaired physical and neurologic development, germ cell mutagenesis resulting in carcinogenesis in subsequent generations) [3]. In a study observing 84 children born from mothers treated with chemotherapy during pregnancy for hematologic malignancies in median follow-up of 18,7 years normal development was observed, with no reports of malignancies [5]. Patients with unfavorable tumor profile should receive adjuvant chemotherapy in the second or third trimester. The most

common regimens are: doxorubicin with cyclophosphamide, 5-fluorouracil, doxorubicin and cyclophosphamide or doxorubicin with vinorelbine. Administration of endocrine therapy during pregnancy is not allowed [3].

The literature reviews indicate that there are unlikely to be serious adverse long-term effects on the fetus, though further studies are needed. Pregnant women should not be denied the potential benefits of chemotherapy [5].

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