Breast Cancer Associated with Pregnancy: Modern Approaches to Diagnosis and Treatment

(Review Article)

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Abstract

Breast cancer is a disease in which abnormal cells in the breast tissue begin to divide uncontrollably and form a tumor. Over the past decades, this pathology has remained the most common malignant neoplasm among women worldwide. Pregnancy at an early age is generally associated with a reduced risk of developing breast neoplasms. However, pregnancy does not always inhibit the growth of tumors, particularly those characterized by a specific hormonal status. This review article is devoted to the study of modern approaches to the diagnosis and treatment of breast cancer in pregnant women and aims to facilitate early detection and prevention of adverse outcomes.

Keywords: pregnancy, breast cancer, diagnosis, mastectomy.

Introduction

Breast cancer (BC) ranks second in incidence and holds a leading position in mortality rates within the fields of oncology and gynecology [1]. According to recent data from the World Health Organization, more than 2.3 million new cases are diagnosed annually. Breast cancer is observed in approximately 1 in 10,000 to 1 in 3,000 pregnancies, most commonly at an average age of around 33 years, and accounts for a significant proportion of overall cancer-related mortality.

In recent years, there has been a noticeable increase in the incidence of breast cancer among young women in their active reproductive period. This trend has led to a growing number of cases diagnosed during pregnancy as well as in the early postpartum period.

In pregnant women, breast cancer is often diagnosed at more advanced stages, which is associated with objective difficulties in its detection. Despite regular medical supervision during pregnancy, the clinical manifestations of the tumor may go unnoticed or be misinterpreted, leading to delayed diagnosis [2].

Objective

The aim of this study is to investigate and analyze the available scientific and literature data on the impact of malignant breast neoplasms on the female body during pregnancy.

Relevance

The relevance of this study is determined by the increasing incidence of breast cancer among women of reproductive age and the growing number of cases diagnosed during pregnancy and in the postpartum period. This issue has a particular importance due to the difficulties of early diagnosis against the background of physiological changes in the breast.

Materials and Methods

The authors of this study conducted a literature review of scientific publications from the past 10 years using the databases eLIBRARY, Google Scholar, CyberLeninka, Science-Education, and Practical Oncology, based on the above-mentioned keywords.

Main Body

In recent years, due to the increasing number of cases of breast cancer diagnosed during pregnancy, the international term pregnancy-associated breast cancer (PABC) has been introduced. This concept encompasses three clinical situations:

• breast cancer diagnosed during pregnancy;
• neoplasm detected during the lactation period;
• breast cancer identified within the first year after the end of pregnancy [3].

Risk factors that increase the likelihood of developing breast cancer include:

• female sex, as the disease occurs significantly more often in women; the male-to-female incidence ratio is approximately 1:135;
• age — the probability of developing the disease increases after 25 years and peaks at 60–65 years;
• reproductive factors — nulliparity, late first childbirth (after 25 years), and a history of abortions;
• hormonal factors, including early menarche (before 13 years) and late menopause (after 55 years);
• ovarian dysfunction, hormonal disorders, and inflammatory diseases of the reproductive system;
• genetic factors — familial breast cancer associated with mutations in the BRCA1 and BRCA2 genes, which significantly increase the risk of developing breast and ovarian cancer [4].

From a *pathogenetic* perspective, pregnancy contributes to a reduced sensitivity of breast cells to oncogenic influences due to hormonally induced differentiation and persistent changes in gene expression. The protective effect is also associated with a decrease in type 1 and type 2 lobules, which are most susceptible to carcinogens, and an increase in type 4 lobules, which have the lowest tumorigenic potential, particularly during lactation. In addition, the overall number of menstrual cycles is reduced.

Early pregnancy (before the age of 20) provides long-term protective effects, whereas later onset of pregnancy is associated with an increased risk of developing breast cancer. Each subsequent pregnancy further reduces this risk.

At the same time, pregnancy may temporarily increase the likelihood of disease progression due to stimulation of the growth of already altered cells, especially in women of advanced reproductive age [5].

The leading complaint in most patients is the detection of a breast lump, which may be accompanied by subjective discomfort in the nipple area, including pain, tingling, and hyperplasia of the gland itself. Nipple retraction and skin changes such as a “orange peel” appearance may also be observed. As the pathological process progresses, asymmetry of the breasts and enlargement of regional lymph nodes are noted [6].

Diagnosis

The *diagnosis* of breast cancer during the gestational period is a challenging task due to anatomical and physiological changes in the breast. During pregnancy, breast tissue becomes denser and more heterogeneous on palpation, which significantly complicates the detection of tumor formations. Increased mammographic density reduces the diagnostic accuracy of mammography, which may yield up to 25% false-negative results; therefore, its use is limited, also taking into account the undesirable radiation exposure.

Radiological imaging methods, including magnetic resonance imaging (MRI), are not recommended as primary diagnostic tools during pregnancy, especially in the first trimester, and should be used with caution.

Ultrasound examination is the method of choice in diagnosis. In combination with Doppler imaging, it allows effective differentiation of breast lesions. Definitive diagnosis is established by ultrasound-guided biopsy (core needle biopsy), which enables confirmation of the diagnosis and performance of immunohistochemical analysis. Cytological methods are less informative due to the high risk of false results [7].

Core needle ("core") biopsy or *excisional biopsy* is performed under local anesthesia. The use of modern biopsy needles with a diameter not exceeding 2 mm makes the procedure less traumatic and psychologically easier to tolerate. It is essential that the pathologist examining the obtained material is informed about the patient's pregnancy [8].

For the detection of distant metastases in the liver and pelvic organs, ultrasound and magnetic resonance imaging are safely used. When performing chest radiography with appropriate shielding, fetal radiation exposure is reduced to approximately 0.00008 Gy, which is significantly below the permissible level (0.05 Gy) [9]. A relatively rarely performed radionuclide bone scan is associated with minimal fetal radiation exposure—about 0.00194 Gy [10].

Bone scintigraphy and positron emission tomography (PET, PET/CT) are contraindicated during pregnancy [11].

Treatment

The management of treating pregnant patients with breast cancer depends on gestational age and the expected timing of delivery, as well as the stage and biological characteristics of the tumor and the presence of comorbidities. In general, the therapeutic approach is similar to that used in non-pregnant patients. Since treatment is feasible starting from the second trimester, diagnosis and therapy should not be delayed, nor should premature delivery be undertaken without sufficient indications [11].

Innovative treatment approaches for breast cancer during pregnancy include:

- surgical treatment;
- chemotherapy.

Radiotherapy, hormone therapy, and targeted therapy are contraindicated during pregnancy [11].

Surgical treatment (mastectomy) can be performed at any stage of pregnancy, provided that anesthesia is properly managed, the mother's condition is stable, adequate oxygenation is maintained, and fetal heart rate monitoring is ensured.

Chemotherapy
Chemotherapy is permissible after the 14th week of pregnancy (starting from the second trimester), except in late gestation (after 35 weeks), and should be completed at least 3 weeks before delivery to allow for hematopoietic recovery. The most well-studied regimens are FAC and AC, while taxanes have been investigated to a lesser extent. To date, there is no reliable evidence of long-term adverse effects in children exposed to chemotherapy in utero.
The use of Tamoxifen is contraindicated at any stage of pregnancy due to the risk of congenital anomalies.
According to the recommendations of the National Comprehensive Cancer Network, radiotherapy is not recommended during pregnancy; therefore, breast-conserving treatment is only possible with subsequent irradiation after delivery. The issue of pregnancy termination is primarily considered when the disease is diagnosed in the first trimester [6].

Conclusion

The development of innovative diagnostic and treatment methods for breast cancer makes it possible to preserve maternal health as effectively as possible while minimizing adverse effects of therapy on the developing fetus. In recent decades, the World Health Organization has increasingly supported a multidisciplinary approach to treatment without termination of pregnancy, which significantly improves survival outcomes for both the mother and the child.

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