CASE REPORT
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Breast cancer during pregnancy: a case series

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ABSTRACT

This study analyzed seven cases of breast cancer diagnosed during pregnancy or within one year of breastfeeding at a private clinic in Teresina (PI), Brazil, between 2012 and 2024. The mean patient age was 33.1 years, with a mean gestational age at diagnosis of 24 weeks. Triple-negative subtype tumors predominated, followed by luminal hybrid and luminal B. Only one patient carried a pathogenic mutation (MUTYH); no BRCA1/2 mutations were identified. Most patients received neoadjuvant chemotherapy with anthracyclines, cyclophosphamide, and taxanes; immunotherapy was used in only one recent case. Surgery was performed in all patients, with a breast-conserving approach in only one. Radiotherapy was indicated for six patients, including axillary treatment in three. No fetal malformations attributable to chemotherapy were observed. Multidisciplinary management allowed all deliveries to occur after fetal maturation, without relevant neonatal complications. One patient with initially metastatic disease achieved complete remission after multimodal treatment and remains without evidence of active disease. Mean overall survival was 85.7 months, with a mean follow-up of 52 months.

KEYWORDS: breast neoplasms; pregnancy; breast feeding; drug therapy; patient care team; treatment outcome.

INTRODUCTION

Breast cancer during pregnancy is an uncommon condition, with reported incidence ranging from 15 to 35 cases per 100,000 pregnancies. The incidence has been increasing because women are becoming pregnant later in life, an age range that also tends to increase the incidence of breast cancer[1]. Triple-negative tumors are more common in this setting. Management is challenging, as it involves decisions about both the mother and the fetus. In general, chemotherapy can be used from the 12th week onwards, surgery may be the initial approach, and radiotherapy should be performed after delivery[2].

CASE REPORT

This is a retrospective cross-sectional study, carried out in a private clinic located in Teresina (PI), with data analysis from 2012 to 2024. Patients diagnosed with breast cancer during pregnancy or within the period of up to one year of breastfeeding were included. The information was obtained through a review of medical records, including demographic data, clinical and histopathological characteristics at diagnosis, therapeutic approaches adopted, recurrences, and survival.

This study is part of a research project approved by the Research Ethics Committee of the Universidade Federal do Piauí (UESPI), under opinion CAAE 30154720.0.0000.5209, and followed the guidelines established by Resolution No. 466/12 of the National Health Council.

During the analyzed period, seven patients were identified with a diagnosis of breast cancer associated with pregnancy or lactation; five were diagnosed during pregnancy and two during breastfeeding. Among the pregnant women, the average gestational age at the time of diagnosis was 24 weeks, ranging from 9 to 36 weeks. The average age of the patients was 33.1 years, ranging from 24 to 36 years.

Four patients presented with triple-negative carcinoma; two were classified as luminal hybrid and one as luminal B. Only two patients reported a family history of breast cancer. However, neither of them carried pathogenic mutations associated with breast cancer. Six of the seven patients underwent hereditary predisposition testing, and only one presented a pathogenic mutation in the MUTYH gene.

Five patients underwent neoadjuvant chemotherapy based on doxorubicin, cyclophosphamide, and paclitaxel. Only one patient received neoadjuvant immunotherapy with pembrolizumab.

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Only one patient underwent surgery during pregnancy, at 16 weeks of gestation, with segmental breast resection and sentinel lymph node biopsy with technetium, followed by adjuvant chemotherapy with the same cytotoxic agents. The newborn showed no abnormalities at birth.

All births occurred via vaginal delivery or cesarean section after fetal maturation, without alterations attributable to chemotherapy, except for one newborn diagnosed with Cri-du-Chat syndrome. Due to having a hormone receptor-positive tumor, she was treated with adjuvant tamoxifen. The patient with a luminal B-shaped hybrid tumor received adjuvant tamoxifen, followed by exemestane in combination with goserelin. Radiotherapy was administered to six patients in the breast and, in three of them, also in the axilla. Of the patients who received axillary radiotherapy, two had positive axillary lymph nodes and one had negative lymph nodes.

A patient presented with liver metastasis at initial assessment and received systemic treatment with trastuzumab, pertuzumab, and paclitaxel, with disease control for 31 cycles. Subsequently, she developed brain metastasis, undergoing neurosurgical resection of the brain metastasis and brain radiotherapy. She then received trastuzumab emtansine and subsequently underwent mastectomy with axillary lymph node dissection and breast reconstruction with a submuscular prosthesis. There was no evidence of metastatic disease on imaging studies at the time of surgery. The patient remains without evidence of active disease 114 months after the initial diagnosis (Table 1).

DISCUSSION

In the present study, the average age of the patients was 33.1 years, with an average gestational age at diagnosis of 24 weeks. These data are consistent with the literature, which reports an average maternal age between 33 and 34 years and an average gestational age at diagnosis ranging from 17 to 25 weeks[3].

Breast cancer during pregnancy is defined as cancer diagnosed during pregnancy or in the first year postpartum[4], representing a diagnostic and therapeutic challenge. Delay in diagnosis is frequent, given the physiological changes in the breast during pregnancy, such as engorgement, hypertrophy, nipple discharge, and increased breast tissue density[5]. Breast cancer is the most frequently diagnosed tumor during pregnancy, reflecting the incidence in women of reproductive age; 10% of cases occur in patients under 40 years of age[6].

The incidence has been increasing because women are increasingly becoming pregnant after the age of 30. Additionally, the implementation of non-invasive prenatal tests, such as ctDNA testing, can result in the incidental detection of maternal malignancies during pregnancy, as can the use of breast ultrasound[7].

It is crucial that the clinician maintain a high index of suspicion for malignancy, and any persistent breast mass lasting more than two weeks during pregnancy should be evaluated by imaging and biopsy. Evaluation of a breast mass by imaging or biopsy should never be delayed because of pregnancy[4]. Pregnant patients with breast cancer may experience symptoms such as a palpable lump or nipple discharge[5]. Recently, Portnow et al.[8] reviewed the guidelines and challenges of mammographic screening in high-risk women during pregnancy and lactation, highlighting that the indication for imaging exams should be individualized and that physiological changes in the breasts can hinder early diagnosis.

Breast ultrasound is the first imaging modality of choice because it does not involve ionizing radiation and allows for the immediate identification of benign lesions, such as cysts and galactoceles, which do not require further evaluation, while a biopsy may be indicated in cases of suspicious lesions. The combined sensitivity and specificity for detecting malignancy in pregnancy are 80.1% and 88.4%, respectively[9].

Computed tomography and bone scintigraphy are not recommended for staging due to the risk of fetal radiation exposure[10].

Table 1. Clinical, therapeutic, and outcome characteristics of the patients (n=7).

Stage	Subtype	NAC	Surgery	Breast Pathology	Axillary Pathology	*Status/months*
IIIA	LB	Yes	BCS + SL	pCR	1+/1	NED/25
IV	LH	-	SM + ALND	NST, G3, tu 3.5 cm	7+/9	NED/114
IIA	TN	Yes	BCS + SL	NST, G3, 2.7 cm	1+/3	NED/80
IIA	TN	Yes	SM +SL+P	pCR	0/3	NED/76
I	LH	Yes	SM+SL+ P	NST, G2, 1.4 cm	1+/1	NED/42
IIB	TN	Yes	BCS + SL	pCR	0/1	Death/19
IIA	TN	Yes	BCS + SL	pCR	0/1	NED/10

NAC: Neoadjuvant chemotherapy; AP: histopathological; LB: Luminal B; LH: Luminal hybrid; TN: triple-negative; BCS+SL: Breast Conserving Surgery with Sentinel Lymph node; SM+ALND: Axillary Lymph Node Dissection; SM+SL+P: simple mastectomy with preservation of the areola-nipple complex with sentinel lymph node and reconstruction with submuscular prosthesis; NST: invasive carcinoma of no special type; pCR: pathological complete response; NED: living without disease.

Treatment decisions should be individualized, taking into account gestational age at diagnosis, disease stage, and patient preferences. Surgery is the first-line treatment and can be safely performed at any gestational stage with minimal complications. The safest time for surgery is the second trimester; in the third trimester, there is an increased risk of premature birth due to surgical stress[11]. Treatment may be conservative or involve mastectomy, depending on the tumor-to-breast ratio, response to neoadjuvant chemotherapy, the presence of pathogenic germline mutations, and the patient's wishes. In the present study, only one patient underwent conservative treatment.

The indications for systemic chemotherapy in pregnancy-associated breast cancer (PABC) are the same as for non-pregnant patients. Chemotherapy should not be administered in the first trimester, as this is when the risk of teratogenic effects is highest[12]. When administered in the second or third trimester, chemotherapy can be adjuvant or neoadjuvant. The reported rate of fetal malformation among those exposed to chemotherapy in the second and third trimesters is approximately 1.3 to 5%, similar to the rate of malformations in fetuses not exposed to chemotherapy[13]. Although studies have demonstrated the relative safety of chemotherapy after the first trimester, exposure to chemotherapy before 12 weeks of gestational age may be associated with major congenital malformations and should be avoided during this period[2].

A multicenter study by Loibl et al.[14] evaluated 447 patients with breast cancer during pregnancy. In this study, 90% of patients who received chemotherapy during pregnancy were treated with anthracyclines (doxorubicin or epirubicin), frequently associated with cyclophosphamide, and a significant proportion also received taxanes (paclitaxel or docetaxel), mainly after the first trimester of pregnancy. The study concluded that these regimens are safe and effective, provided they are initiated after the first trimester, and that treatment should be as similar as possible to the standard for non-pregnant patients. The estimated five-year overall survival rate was 77% for women who received chemotherapy during pregnancy and 82.4% for those who received it after delivery or with treatment interruption.

In our study, two patients received a diagnosis of breast cancer while breastfeeding. The literature indicates that breast cancer diagnosis during lactation is rare, and there is no evidence that it is more common during this period compared to other times in reproductive life. Recent studies have highlighted that breast cancer during pregnancy and lactation is uncommon, but diagnosis is often delayed due to physiological changes in the breasts and lower clinical suspicion, which can lead to presentation at more advanced stages[15]. Therefore, the incidence is not higher during breastfeeding, but recognition can be more difficult[16].

In our study, all children were born after fetal maturation, without malformations attributable to chemotherapy; there was one case of Cri-du-Chat syndrome, whose relationship with chemotherapy is unlikely, since the exposure occurred after the first trimester (in the third trimester) and the literature points to a sporadic origin of this syndrome, without proven causal relationship with maternal exposure to chemotherapy during pregnancy, especially when the exposure occurs after the first trimester[17].

Neoadjuvant immunotherapy was applied only to the patient diagnosed in 2024, when the drug (pembrolizumab) was already available through the health plan. In the other patients, the drug was not available or the insurance company did not authorize its use. The Keynote-522 study demonstrated that the addition of pembrolizumab to neoadjuvant chemotherapy significantly increases the pathological complete response rate in locally advanced triple-negative breast cancer and improves event-free survival compared to chemotherapy alone. The pCR rate was approximately 65% in the group that received the combination, versus 51% in the control group, and the five-year event-free survival was 86.6%, compared to 81.2% for chemotherapy alone[18]. A recent meta-analysis confirms that neoadjuvant immunotherapy, when combined with chemotherapy, improves the prognosis of triple-negative breast cancer, increasing cure rates and reducing the risk of progression[19].

The case presented in our series, of a patient with metastatic breast cancer to the liver at initial diagnosis, who achieved complete remission after multimodal treatment, finds support in recent literature. In the report by Aktoz et al.[20], a pregnant patient with HER2-positive breast cancer and massive liver metastasis was treated with trastuzumab and docetaxel during pregnancy, resulting in complete remission of liver lesions, as confirmed by postpartum imaging studies. After completion of systemic treatment, the patient underwent mastectomy, also without evidence of residual disease, and remained recurrence-free during the reported follow-up.

The study conducted by our institution has significant limitations due to the small number of cases included, which prevents the evaluation of prognostic factors associated with survival.

CONCLUSION

In the present study, the overall survival of patients with breast cancer diagnosed during pregnancy or breastfeeding was 85.7 months, with a mean follow-up of 52 months.

AUTHORS' CONTRIBUTIONS

SCC: Conceptualization, Data curation, Writing – first draft, Investigation, Visualization. SCV: Project management, Formal analysis, Writing – revision and editing, Methodology, Supervision, Validation.

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