CASE REPORT
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Invasive ductal carcinoma of the breast in a pregnant woman: case report

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ABSTRACT

Gestational breast cancer is the most common cause of cancer in pregnant women. It is a challenging condition for the medical team, since the physiological changes in the breast during this period increase the density of the breast parenchyma, which makes it difficult to detect the nodule on physical and imaging examination, causing delay in diagnosis. We present here a case report of a woman with breast cancer diagnosed during pregnancy. This was a 28-year-old female patient who arrived at the service at 14 weeks' gestation, diagnosed with invasive ductal carcinoma in the left breast, with T4dN2M0 staging. Neoadjuvant chemotherapy treatment was started with a pause for the cesarean section at 36 weeks' gestation. After delivery, chemotherapy was restarted, followed by radical mastectomy, radiotherapy and hormone therapy. Two years after the initial diagnosis and still being treated with hormone therapy, the patient presented with musculoskeletal pain, detected on magnetic resonance imaging and bone scintigraphy, as well as several points of metastasis in the spine with pathological fracture of L2-L3, where she was then submitted to decompressive laminectomy. After surgery, radiotherapy of the thoracic and lumbar spine was started, in addition to chemotherapy. Currently, the patient is asymptomatic, being on paclitaxel and transtuzumab, with stable bone scintigraphy and radiography and ultrasound showing no metastases, and the child is healthy after three years of follow-up.

KEYWORDS: pregnant woman; breast cancer; invasive ductal carcinoma; pregnancy.

INTRODUCTION

Gestational breast cancer is diagnosed during pregnancy or up to one year after delivery, where it is the most common cause of cancer in pregnant women, followed by cervical cancer, leukemia, melanoma and lymphomas[1]. The incidence varies between 0.02% and 3.8% of pregnancies, with a frequency of one case in every thousand pregnancies. Women over 35 years of age are at greater risk, and with the current lifestyle of postponing pregnancy to the third and fourth decades, the number of cases tends to increase[2].

No histological differences in breast cancer have been identified between pregnant and non-pregnant women. Therefore, the most common type is ductal, followed by lobular, while the mucinous, papillary, medullary and tubular types are less frequently found. However, among pregnant women, the tumors are usually larger and are associated with high lymph node involvement[3].

Some reported studies on the subject point to the breast lump as the main complaint of the patient, with the exception of the work published in BMC Women's Health, which presents a case of breast cancer in a pregnant woman whose only symptom was low back pain, where bone metastasis was later revealed. Another similarity between the studies already published concerns the delay in the diagnosis of this cancer in this specific group of patients, due to the difficulties encountered in performing imaging tests that emit radiation during pregnancy and the physiological changes in the breast during this period[4-8].

Breast cancer occurs rarely during the pregnancy-puerperal cycle, even though it is the most common malignancy in pregnant women. However, studies show that its incidence has increased in recent years. In this context, as it is an uncommon disease, there are few studies on the subject, with little known about its etiology, and treatment decisions are mostly derived from large trials in non-pregnant women[2].

Therefore, with the identification of a confirmed case, its documentation is considered of great importance to identify possible correlated risk factors, develop more specific therapeutic strategies and even design future prevention measures. Therefore, the aim of the present study was to report

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the case of a pregnant patient diagnosed with breast cancer, including her clinical history, histological subtype and course of treatment.

CASE REPORT

A female patient, 28 years old, 14 weeks pregnant, was seen at the cancer hospital of a city in the countryside of São Paulo State, Brazil in March 2018, complaining of a lump in the left breast. After core needle biopsy, the patient was diagnosed as having invasive ductal carcinoma of the left breast. On physical examination, she had an extensive area of *peau d'orange* skin edema on the left breast, globally indurated with a 12.5-cm nodular mass predominantly in the upper inner and upper outer quadrants and an axillary mass on the left compatible with coalescing lymph nodes. Core biopsy was performed, which showed grade III invasive ductal carcinoma (SBR) with vascular and lymphatic invasion. The immunohistochemical study demonstrated estrogen and progesterone receptors in 90% of cells, human epidermal receptor (HER2) positive (3+) and 80% Ki67 staining. Screening tests for metastases were requested, namely chest X-ray and abdominal ultrasound, which did not demonstrate expansive lesions in the evaluated areas or any changes. Thus, the initial clinical staging as T4dN2M0 was completed.

The therapeutic plan applied consisted of weekly neoadjuvant chemotherapy with paclitaxel (12 sessions), followed by four cycles of doxorubicin (A) and cyclophosphamide (C), interruption of preterm pregnancy with discontinuation of breastfeeding, surgical treatment, transtuzumab, radiotherapy and hormone therapy.

In August 2018, after 12 sessions of paclitaxel and three cycles of AC, with the last one at the end of July, the patient, with a gestational age of 36 weeks, underwent cesarean section, resulting in a live newborn without abnormalities. Cabergoline was prescribed for lactation inhibition, and breastfeeding was prohibited from the first postpartum moment. The patient was discharged with the newborn.

Twenty-five days after delivery, the patient underwent the last AC cycle. She then returned for preoperative evaluation, where a radical mastectomy with left axillary dissection was proposed. On physical examination, she showed clinical remission of the cancer, so preoperative tests were requested. After a few days, the patient came to the outpatient clinic with the results of these tests showing normal parameters. On clinical examination, she had an enlarged left breast, with bulging in the upper outer quadrant, diffuse nodular mass reaching almost all quadrants of the breast and an axillary lymph node on the left with fibroelastic consistency. On that day, the patient was referred for the proposed surgery, which was performed after six days. The histopathological examination showed the presence of invasive ductal carcinoma grade III SBR (architectural grade 3, nuclear 3, mitotic 3), measuring 13.5 cm in the longest axis and with vascular and lymphatic invasions present, skin and nipple infiltrated by the neoplasm, anterior surgical margin exiguous, cutaneous lymphatic emboli close to the margin, deep margin 2.5 mm apart, other margins free, metastases to 4 of 25 dissected lymph nodes, and pathological staging pT4B, pN2a. She was referred for follow-up with clinical oncology and physical therapy. In the same month, the use of leuprolide acetate combined with anastrozole and radiotherapy was started, followed by transtuzumab.

The patient remained asymptomatic until June 2020, when she was admitted to the emergency department reporting migratory and additive polyarthralgia for three months, with significant worsening in the previous two weeks, starting in the cervical spine joints and progressing to hand arthralgia and, soon after, hip arthralgia. The patient denied fever and joint swelling and reported loss of strength in the lower limbs, accompanied by persistent low back pain of severe intensity. Magnetic resonance imaging of the lumbar spine was performed, which showed a pathological fracture of L2-L3, with spinal cord compression and paravertebral extension, in addition to a fracture of L5, with a marked reduction in the height of the vertebral body, possibly indicating a lumbar metastasis. Also in June 2020, the patient underwent L1-L5 decompressive laminectomy, with subtotal removal of the neoplastic lesion and spinal canal decompression, in addition to pedicle fixation T11- L4 -L5.

After surgery, radiotherapy of the thoracic and lumbar spine was started, as well as treatment with capecitabine 500 mg, zoledronic acid and transtuzumab. In November, bone scintigraphy was requested, which showed progression of the bone lesion. Capecitabine was then discontinued, while zoledronic acid and transtuzumab were maintained, and paclitaxel was started.

Currently, the patient is asymptomatic on paclitaxel and transtuzumab, with stable bone scintigraphy and radiography and ultrasound without metastases. The child is healthy, now three years old.

DISCUSSION

In this article, we present a patient diagnosed with breast cancer detected during pregnancy, whose treatment was difficult and thus progressing to bone metastasis.

Gestational breast cancer has a clinical history similar to that of non-gestational breast cancer. There may be skin changes, hemorrhagic nipple discharge, enlargement of the affected breast, and most often the presence of a painless lump[2,9].

The diagnosis is made with the detection of the nodule in the physical examination of the breasts or in the ultrasound examinations of the breasts and mammography, and it should be confirmed preferably by core biopsy[10]. However, the detection of the nodule during pregnancy is hampered by the physiological

changes of pregnancy, which respond to the increase in the level of circulating hormones, causing intense ductal proliferation, lobular growth, fibroglandular enlargement of the parenchyma and glandular vascularization. These changes generate an increase in the density of the breast parenchyma, making it difficult to identify changes both in the physical examination and in the imaging tests, which can be difficult to interpret. As a result, there is an average delay of two months in the diagnosis of breast cancer in pregnant women[2].

For additional investigation of a palpable mass on physical examination in a patient who is pregnant or not, the main tests used are breast ultrasound and mammography, which are sensitive in the identification and characterization of nodules and lymph nodes, both being safe during pregnancy. After diagnosis, it is important to perform disease staging tests. The main classification used is the Classification of Malignant Tumors (TNM), which is based on the size of the nodule (T), the number of affected lymph nodes (N) and the presence of metastases (M). In turn, for the definition of T and N, the tests mentioned above are used. In the investigation of metastases, in general, computed tomography of the chest and abdomen and bone scintigraphy are used, tests that can be replaced by PET-Scan (PET/CT). In pregnant women, however, cumulative fetal exposure to radiation above 100 mGy should be avoided, given the risk of congenital malformations and miscarriages. Thus, examinations with greater radiation, such as tomography, scintigraphy and PET-Scan, should be replaced by those that do not expose the fetus to radiation, such as abdominal ultrasound and spinal magnetic resonance, the latter used only if the patient complains of back pain. Chest X-ray is also safe in the investigation of metastases during pregnancy, because despite using ionizing radiation, it has low levels, so it is not harmful to the fetus if used with caution[11].

First-line treatment remains radical mastectomy, and its indications follow the same criteria for performing it outside the pregnancy period[10]. Adjuvant chemotherapy is usually necessary in these cases, as they are young patients and, consequently, have greater tumor aggressiveness[2]. The therapeutic regimen most commonly used in pregnant women is based on doxorubicin, cyclophosphamide and paclitaxel (AC-T) or 5-fluorouracil, doxorubicin and cyclophosphamide (FAC). Both regimens can be performed in the second and third trimesters of pregnancy and should be avoided during the first trimester and in the three to four weeks before delivery, as they are associated with fetal malformations and transient fetal myelosuppression, respectively[1,2]. Neoadjuvant treatment is reserved for cases of local recurrence and locally advanced or metastatic carcinoma[6].

Anti-HER2 therapy is indicated for patients with overexpression of this receptor, with trastuzumab being one of the drugs used. However, all drugs in this class, if administered during pregnancy, can cause complications such as oligohydramnios, fetal pulmonary hypoplasia and developmental abnormalities, so their use should be postponed to the postpartum period, which was performed in the study patient[8]. Another adjuvant therapy widely used to prevent recurrence of hormone-sensitive breast cancer is tamoxifen, but it is also a contraindicated drug during pregnancy because it presents a high risk of congenital abnormalities, miscarriages and stillbirth[12]. Although reports regarding the use of tamoxifen during pregnancy are scarce, in a study with pregnant mice injected with tamoxifen, morphological defects were observed in most of the evaluated animals, including pericardial edema, cleft palate, neural tube defects, necrotic embryos and ophthalmic defects. In addition, the mother displayed deleterious effects, the most common being uterine bleeding[13].

Furthermore, the patient should not breastfeed while being treated with these drugs[6]. Radiotherapy is also contraindicated during pregnancy because of fetal exposure to radiation, and should, if necessary, be performed in the postpartum period[14].

In the case reported, the patient was given paclitaxel, doxorubicin and cyclophosphamide as neoadjuvant therapy, as she had a locally advanced tumor. After delivery, the treatment was continued with the planning of the mastectomy and the use of radiotherapy and hormone therapy.

Prognosis depends on factors such as: patient age, tumor staging, histological grade and HER2 status. In addition, breast cancer during pregnancy is associated with worse survival[15].

CONCLUSIONS

The incidence of breast cancer during pregnancy shows an increasing trend for numerous reasons, the main one being the postponement of pregnancy. Despite this increase in cases, the difference in time of diagnosis between pregnant and non-pregnant women is still divergent, being earlier in non-pregnant women[16]. To reduce this difference and diagnose breast cancer earlier during pregnancy, it is critical that clinical breast examination be performed in every prenatal visit, in a routine way, with the aim of detecting possible gland changes.

The hormonal changes of pregnancy, as mentioned above, lead to greater difficulty in diagnosis by clinical examination, and in doubtful cases, investment in breast ultrasound can be useful, contributing to a diagnostic advance in this group of patients.

AUTHORS' CONTRIBUTION

MPPB: Data curation, Funding, Investigation, Methodology, Visualization, Writing – original draft. MBC: Conceptualization, Formal analysis, Methodology, Project administration, Supervision, Validation, Visualization, Writing – review & editing. ELD: Formal analysis, Methodology, Supervision, Validation, Visualization, Writing – review & editing.

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