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## Case Report

# Giant triple negative pregnancy-associated breast cancer (PABC) in a young woman: From diagnosis to therapy step by step: A case report <sup>☆</sup>

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## ABSTRACT

Pregnancy-associated breast cancer (PABC) presents unique challenges. This type of breast cancer is often more aggressive than that diagnosed in nonpregnant women, and its diagnosis is frequently delayed. Several factors contribute to this delay, including the physiological changes that occur during pregnancy, such as breast enlargement, breast tenderness and increased tissue density, which can mask early signs of malignancy. Additionally, a lack of awareness among healthcare providers can lead to symptoms being dismissed as normal pregnancy-related changes, and then being underestimated. Consequently, PABC is often diagnosed at more advanced stages, which can result in a poorer prognosis for the patient. This case study reports a 36-year-old woman in good general health, who received histological diagnosis of breast cancer during her pregnancy after presenting for self-detection of an enormous palpable breast mass. Prior to hospitalization, the patient had been treated with antibiotics in the mistaken belief that it was infectious mastitis; subsequently, considering the huge dimensions of the mass and the presence of lymph node metastases, neoadjuvant chemotherapy was started until induction of labor. Imaging techniques such as ultrasonography (and mammography as an adjunct) and nonenhanced MRI (due to potential toxicity of gadolinium to the fetus) can be used for staging maternal breast disease during pregnancy. A multidisciplinary approach which involves the radiologist, the breast surgeon, the oncologist and the gynecologist is fundamental to ensure the best prognostic outcomes for both the mother and the fetus.

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## Introduction

Pregnancy-associated breast cancer (PABC) is typically defined as breast cancer occurring during pregnancy, usually within 1 year postpartum, or during lactation [1].

Although pregnancy and the postpartum period are intertwined, evidence suggests that breast cancer during pregnancy (PrBC) should be considered a distinct entity from breast cancer occurring during the postpartum period (PPBC), which can extend up to 5–10 years after birth.

This differentiation is important due to the differing prognoses. In fact, studies show that PrBC has a prognosis comparable to that of breast cancer occurring in young, nonpregnant women. In contrast, PPBC is linked to poorer survival rates and a more than 2-fold increased risk of metastasis compared to breast cancer diagnosed at other points in a woman's lifetime [2].

The incidence has varied among different studies from 1:10,000 to 1:3000 of all pregnancies, with a median age at diagnosis of 33 years. The rate of PABC among pregnant women aged < 45 years has varied from 2.6% to 6.9%. In contrast, in those aged < 35 years, the rate has been 15.6% of all BC cases. However, this incidence may rise due to trends of delaying pregnancy to older ages [3].

A large recently published cohort study by Amant et al. (2021) showed that pregnant patients were more likely to have hormone receptor-negative tumors or triple-negative breast cancer (TNBC) than patients without associated pregnancy [4]. According to some Authors (Amant, Schedin et al.) [2], in the future a separate and in-depth investigation of both entities (PrBC and PPBC) will be necessary in order to improve our understanding of the biology of breast cancer during the different periods of the maternal life (pregnancy, lactation, involution), and will help us to reach new developments in tumor biology knowledge.

## Case presentation

A 36-year-old primiparous woman, at 28+1 weeks of gestational age, presented on June 6, 2024 to our Hospital with a huge palpable mass in her right breast. She had used oral contraceptives for 7 years and had no family history of breast cancer, but had a positive medical family history of colon, hepatic and kidney cancers. The general practitioner was treating her with antibiotics (amoxicillin) on the assumption that it was infectious mastitis, before referring her to the Emergency Room.

Clinical examination revealed the right breast grossly enlarged due to the presence of a mass filling the entire right breast, with associated skin ulcers exuding serous material. Right breast ultrasound identified a solid irregular mass extending throughout the entire right breast, with multiple enlarged lymph nodes in the ipsilateral axilla. These findings were classified as BI-RADS category 5 according to Breast Imaging Reporting and Data System (ACR BI-RADS, fifth edition).

The patient was advised to stop amoxicillin and underwent a right breast ultrasound-guided core biopsy, and histopatho-

logical results indicated high-grade invasive “triple negative” lobular carcinoma, negative for estrogen receptor, progesterone receptor and HER2, with less than 5% of intermediate-grade ductal carcinoma, intralesional sclerosis and necrosis. The lymph nodes were positive, and the assessed clinical stage was cT4cN3.

A whole-body magnetic resonance imaging (MRI) was performed to rule out the presence of metastatic lesions. Due to the potential toxicity of gadolinium to the fetus and in accordance with the patient's preferences, the diagnostic procedure was conducted without the administration of a contrast agent, with the purpose of using the performance of the DWI sequences. Italian guidelines drawn up by AIFA (“Agenzia Italiana del Farmaco”, the Italian Medicines Agency) suggest that gadolinium should not be used during pregnancy unless magnetic resonance imaging with contrast medium is essential, and suitable alternatives are not available, this because of the potential higher frequency of stillbirth or neonatal death [11].

The whole-body MRI without contrast showed a right breast mass measuring 19 × 15 cm, with multiple omolateral right axillary, supraclavicular and internal mammary chain lymphadenopathies, the largest being 9 cm. The Diffusion Weighted Imaging (DWI) sequences unfortunately were burdened by artifacts due to suboptimal adhesion of the surface coil to the pregnant abdomen, and did not demonstrate any sure evidence of secondary disease localizations. Following a multidisciplinary discussion, neoadjuvant chemotherapy with Epirubicin was initiated at 31 weeks of pregnancy and was discontinued 2 weeks before planned induction of childbirth, which was scheduled for July 31, with cesarean section. During the neoadjuvant treatment, the patient did not face physical complications, except a little serous exudation from the breast lesion. Furthermore, she was assisted with frequent psychological counseling which reported a proactive and resilient behavior of the woman, describing herself as compliant with the proposed treatment path and also comforted by the multidisciplinary care taken by the medical team.

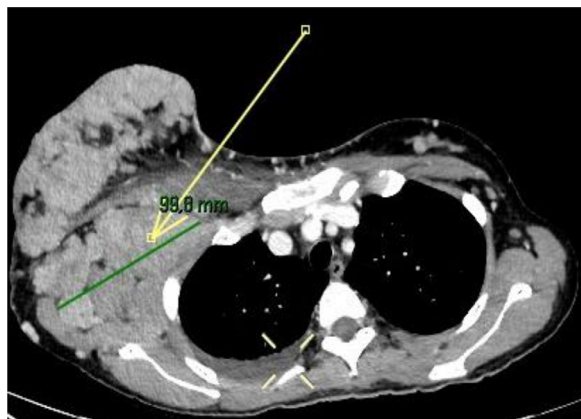
In the postpartum, a contrast enhanced total body CT was performed, with the evidence of multiple disease localizations in the contralateral left breast across all quadrants (Figs. 1–3), and the finding of the presence of secondary disease localizations in other organs such as liver. These findings were confirmed by a subsequent abdominal contrast-enhanced MR which revealed some small occult secondary disease localizations in the liver (Fig. 4), pancreas (Fig. 5), peritoneum (Fig. 6) and even bones (Fig. 7). Given the extent of the disease, a postpartum neoadjuvant chemotherapy regimen with Carboplatin and Paclitaxel was planned.

## Discussion

Usually, breast cancer during pregnancy presents with a painless palpable mass (90%) or thickening of the skin. Lymph nodes involvement and inflammatory changes are expected at diagnosis [5]. Diagnosing breast cancer during pregnancy presents challenges. Delays in the diagnosis of PABC are likely



**Fig. 1** – This contrast-enhanced CT scan shows a large mass with heterogeneous contrast enhancement (CE) in the right breast, infiltrating the chest wall and skin. Right-side pleural effusion is present, with atelectasis of the adjacent lung parenchyma.



**Fig. 2** – This CE-CT scan reveals multiple and confluent lymphadenopathies extending from the right supraclavicular region to the omolateral axillary area, completely occupying the axillary space.



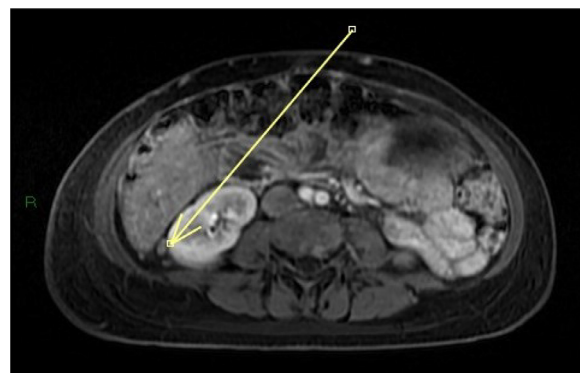
**Fig. 3** – This CE-CT scan shows multiple hyperdense nodular suspicious lesions located in all quadrants of the contralateral left breast.



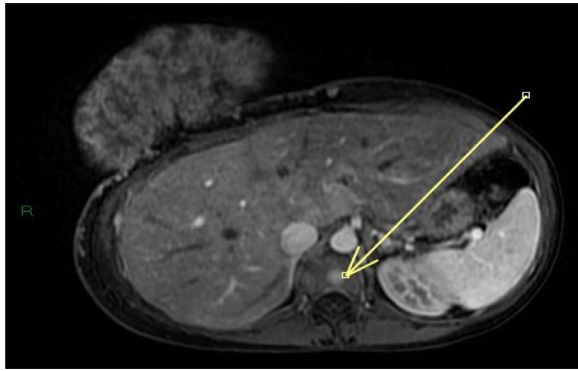
**Fig. 4** – Hyperintense area after the administration of contrast agent (gadolinium) at MRI in the liver, compatible with disease localization. The DWI sequence demonstrated other small areas of signal restriction in the liver, substantial with hepatic metastasis.



**Fig. 5** – Hypointense area in the pancreatic tail after the administration of contrast agent (gadolinium) at MRI, compatible with secondary disease localization.



**Fig. 6** – This CE-MRI scan demonstrates a nodular image located along the right posterior pararenal fascia, compatible with a small peritoneal disease localization.



**Fig. 7 – This CE-MRI shows a faint hyperintense area within the vertebral body after the administration of contrast agent, compatible with bone disease localization.**

due to physiological pregnancy-induced breast changes; in fact, during pregnancy, there are several modifications of the breast tissue that may mask initial signs of breast cancer [6].

Ultrasound (US) is the first-line imaging modality in women with suspected PABC, with reported high sensitivity and negative predictive values [5].

According to the latest American College of Radiology (ACR) appropriateness criteria, mammography is usually appropriate and should be used as an adjunct to US [7]. Mammography is virtually not contraindicated during pregnancy, as the radiation dose from a bilateral 2-view standard mammogram is <3 mGy per view. The ACR and the Society for Pediatric Radiology state that there aren't demonstrated deterministic effects, such as teratogenesis, below a threshold of 50 mGy [8].

Contrast-enhanced (CE) breast MRI is not considered a safe modality during pregnancy, due to fetal safety concerns associated with gadolinium-based contrast agents, which are known to cross the placenta. In fact, the contrast agents are classified as type C drugs, according to the FDA. In recent years, novel un-enhanced functional techniques such as diffusion-weighted imaging (DWI) have had an increasing role as a valuable diagnostic tool during pregnancy, in order to facilitate an earlier diagnosis of PABC [9].

This case report depicts an advanced stage of metastatic disease, where the spread to organs such as the liver and the pancreas became apparent (Figs. 4 and 5). Additionally, peritoneal involvement was confirmed, as previously identified through a postpartum CE-CT (Fig. 6). The CE-MR imaging also revealed a significant and widespread involvement of the bones with numerous secondary disease sites (Fig. 7).

These findings point to an extensive and aggressive progression of the disease, underscoring the challenges in managing such complex cases, especially given the limitations of imaging during pregnancy. Although there is some variability in the literature, PABC typically carries a worse prognosis compared to nonpregnancy-associated breast cancer. It often exhibits aggressive characteristics, including a younger age at diagnosis, advanced local stage, negative hormone receptor status or overexpression of Human Epidermal Growth Factor Receptor 2 (HER2), lymph-vascular invasion (LVI) and lymph

nodes involvement [6]. The management of PABC can be complicated or delayed due to the following obstetric considerations; chemotherapy can be administered during the second and third trimesters, but radiotherapy, hormone therapy, and biological agents are generally contraindicated during pregnancy [10].

## Conclusions

The management of breast cancer during pregnancy presents substantial challenges. Pregnancy-associated breast cancer (PABC) generally has a poorer prognosis, partly due to both the delay in diagnosis and the limitations in treatment options. Imaging techniques such as ultrasonography (and mammography as an adjunct) and nonenhanced MRI (due to some concerns about the potential toxicity of gadolinium to the fetus) are used to assess and stage the local extent of the disease during pregnancy. A multidisciplinary approach is crucial to ensure the best prognostic outcomes, for both fetal health and maternal cancer management.

## Patient consent

This is to state that the patient gives full permission for the publication. Complete written informed consent was obtained from the patients for the publication.

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