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(PERSPECTIVE ARTICLE)

Pregnancy-associated breast cancer at term: Vitamin D deficiency and a missed diagnostic window in pregnancy-associated malignancy

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Abstract

Pregnancy-associated breast cancer (PABC), defined as breast cancer diagnosed during pregnancy or within one year postpartum or any time during lactation, represents a distinct clinical challenge due to physiological breast changes that may obscure malignant findings and contribute to diagnostic delay. While increasing attention has been paid to breast cancer diagnosed during early and mid-pregnancy, malignancy presenting at term or in the immediate peripartum period remains comparatively under-explored.

This Perspective uses a real-world clinical case diagnosed at term as a conceptual framework to highlight the peripartum period as a critical but often overlooked diagnostic window in pregnancy-associated malignancy. The case illustrates how persistent breast symptoms in late pregnancy may be misattributed to physiological changes, leading to delayed imaging and diagnosis despite frequent healthcare contact. In addition, the concurrent finding of severe maternal vitamin D deficiency (VDD) raises biologically plausible questions regarding its potential role in tumor behavior within the unique hormonal and immunological milieu of pregnancy.

Beyond the individual clinical scenario, this article discusses broader implications for obstetric and oncologic practice, emphasizing the importance of maintaining a high index of suspicion for unilateral or progressive breast findings regardless of gestational age. The safety and accessibility of breast ultrasound during pregnancy support its use as a first-line diagnostic tool, including in late gestation. Multidisciplinary collaboration is essential to ensure timely diagnosis and to balance maternal oncologic management with fetal and neonatal safety.

By drawing attention to diagnostic vulnerability at the time of delivery, this Perspective aims to promote earlier recognition of pregnancy-associated breast cancer and to encourage further research into modifiable biological factors, such as vitamin D status, that may influence disease presentation and outcomes.

Keywords: Pregnancy-associated breast cancer; Peripartum period; Diagnostic delay; Vitamin D deficiency; Breast ultrasound; Multidisciplinary care

1. Introduction

Pregnancy-associated breast cancer (PABC), defined as breast cancer diagnosed during pregnancy or within one year postpartum, remains a distinct clinical entity associated with diagnostic delay and adverse outcomes compared with breast cancer in non-pregnant women (1,2). Physiological breast changes during pregnancy, including glandular hyperplasia, increased vascularity, and nodularity, may obscure malignant lesions, particularly in late gestation (3).

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While breast cancer diagnosed during early or mid-pregnancy has been extensively described, malignancy identified at term or in the immediate peripartum period remains under-discussed.

Here, we present a real-world case of breast cancer diagnosed at term, using it as a narrative clinical anchor to underscore the peripartum period as a critical but frequently overlooked diagnostic window in pregnancy-associated breast cancer. Within this context, we also examine the concurrent finding of severe maternal vitamin D deficiency and discuss its potential biological and clinical relevance.

2. A clinical anchor: breast cancer diagnosed at term

A 32-year-old primigravida presented at 38 weeks of gestation with a painless palpable mass in the left breast. The mass had been noticed approximately three weeks prior and was initially attributed to physiological breast changes of late pregnancy. The pregnancy had been otherwise uncomplicated, and the patient had no significant medical history or family history of breast or ovarian cancer.

On clinical examination, a firm, non-tender, mobile mass measuring approximately 2.5 cm was palpated in the upper outer quadrant of the left breast. No skin changes, nipple retraction, or pathological nipple discharge were observed, and no clinically palpable axillary lymphadenopathy was detected.

Breast ultrasound revealed a 2.5 × 2.3 cm hypoechoic lesion with irregular margins and posterior acoustic shadowing, classified as BI-RADS 5. Ultrasound-guided core needle biopsy confirmed invasive ductal carcinoma, histological grade II, estrogen receptor positive (90%), progesterone receptor positive (70%), and HER2 negative (0 by immunohistochemistry), with a Ki-67 proliferation index of 22%..

Laboratory evaluation at presentation demonstrated severe maternal vitamin D deficiency, with serum 25-hydroxyvitamin D levels of 8.6 ng/mL (reference range: 30–50 ng/mL), indicating profound vitamin D deficiency. Additional laboratory findings revealed mild gestational anemia (hemoglobin 11.2 g/dL), normal leukocyte count (9.8 $\times 10^9$/L), and normal platelet count (245 $\times 10^9$/L). Serum biochemistry showed normal calcium (9.1 mg/dL), phosphate (3.4 mg/dL), and parathyroid hormone levels (52 pg/mL), with mildly elevated alkaline phosphatase (145 U/L), consistent with physiological changes of late pregnancy.

The patient was discussed at a multidisciplinary tumor board involving obstetrics, breast surgery, medical oncology, and neonatology. Given the advanced gestational age, definitive oncologic treatment was planned immediately postpartum. Vitamin D supplementation was initiated (cholecalciferol 1,000 IU daily), and close obstetric surveillance was maintained.

The patient delivered a healthy neonate at 38+4 weeks of gestation. Postpartum staging investigations, including chest radiography and abdominal ultrasound, revealed no evidence of distant metastatic disease.

2.1. Diagnostic delay at the end of pregnancy

Diagnostic delay is a well-established feature of PABC and has been associated with more advanced disease at diagnosis and poorer prognosis (2,4). The peripartum period represents a particularly vulnerable diagnostic blind spot. Breast symptoms arising late in pregnancy may be deprioritized as clinical attention shifts toward imminent delivery, while early postpartum lactational changes further complicate breast assessment for both patients and clinicians.

However, breast ultrasound is safe, widely available, and recommended as the first-line imaging modality during pregnancy and lactation (5). Persistent, unilateral, or progressive breast masses should prompt timely imaging regardless of gestational age. In the present case, the three-week interval between symptom onset and diagnostic imaging represents a missed opportunity for earlier evaluation during a period of frequent healthcare contact, potentially delaying diagnosis until the postpartum period, when tumor burden may be greater and treatment decisions more complex.

2.2. Vitamin D deficiency as a concurrent finding

Severe maternal vitamin D deficiency was identified at the time of cancer diagnosis in this patient. Vitamin D deficiency is highly prevalent among pregnant women, including in Southern Europe and Mediterranean regions, despite adequate sunlight exposure (6). Pregnancy itself is associated with increased vitamin D demands, and deficiency has been linked to immune dysregulation and altered inflammatory responses. Emerging evidence suggests that vitamin D may

influence breast cancer biology through modulation of cellular proliferation, apoptosis, angiogenesis, immune regulation, and tumor microenvironment dynamics (7,8).

Although causality cannot be inferred from a single case, the coexistence of pregnancy-associated breast cancer (PABC)and profound vitamin D deficiency raises important questions regarding tumor behavior within the unique hormonal, metabolic, and immunological milieu of pregnancy.

The normal calcium–phosphate–PTH axis observed in this patient underscores the silent nature of vitamin D deficiency and highlights the potential value of biochemical assessment in selected high-risk clinical contexts. While routine screening for vitamin D deficiency in PABC cannot be recommended based on isolated observations, this finding supports further investigation in systematically designed studies.

2.3. Implications for obstetric and oncologic practice

This perspective highlights the importance of heightened clinical vigilance for breast symptoms during late pregnancy. Obstetricians, midwives, and clinicians providing antenatal care should maintain a low threshold for imaging evaluation when breast complaints persist, even close to delivery. Persistent, unilateral, or progressive breast masses should not be dismissed as physiological without appropriate evaluation, regardless of gestational age.

Once malignancy is suspected or confirmed, multidisciplinary collaboration is essential. Early involvement of breast surgeons, oncologists, and neonatologists allows for individualized management plans that optimize maternal outcomes while ensuring fetal safety (1,9). In the present case, integrated management facilitated timely diagnosis, safe delivery, and prompt postpartum oncologic staging.

2.4. Future directions

As maternal age at first pregnancy continues to rise globally, the incidence of pregnancy-associated malignancies is expected to increase (10). Prospective studies are needed to better characterize diagnostic delays occurring at term and in the peripartum period. In addition, the potential role of modifiable biological factors, such as vitamin D status, warrants further exploration in larger cohorts of pregnant patients with breast cancer (PABC).

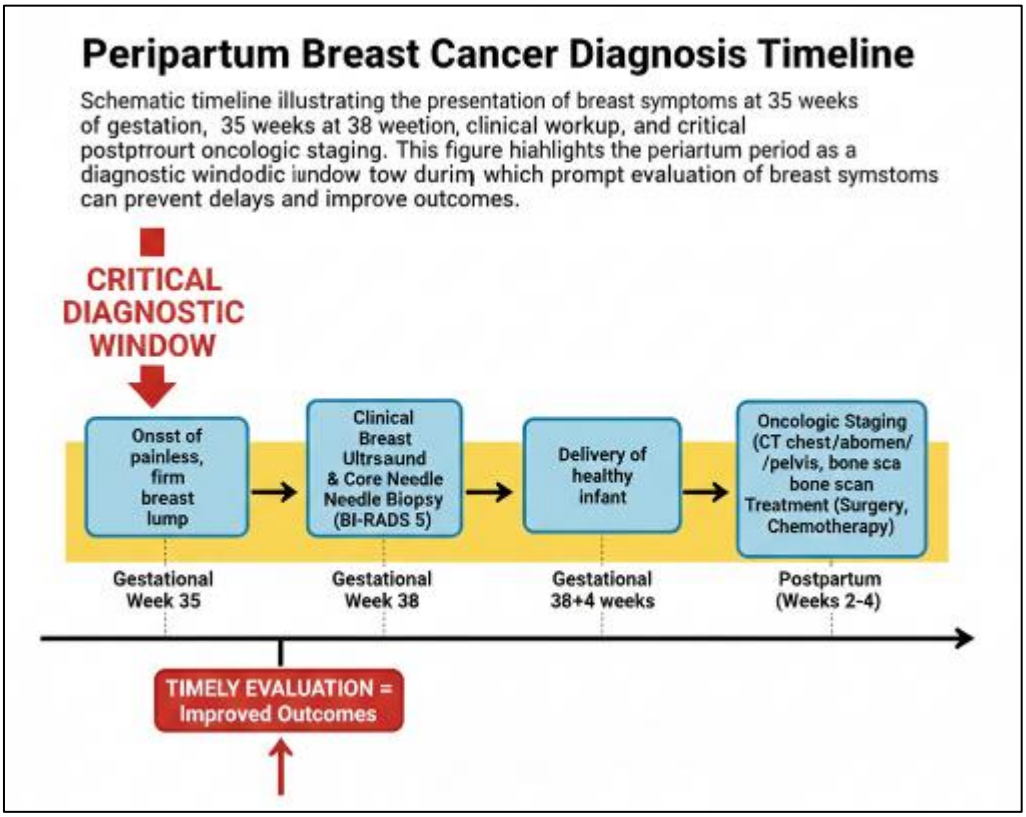

Figure 1 Timeline of symptom onset, diagnostic evaluation, and delivery in pregnancy-associated breast cancer diagnosed at term

3. Conclusion

Breast cancer may present during late pregnancy and can be easily overlooked due to physiological breast changes and competing clinical priorities at term. This perspective identifies the peripartum period as a critical diagnostic window and underscores the need for prompt evaluation of persistent breast findings regardless of gestational stage. The concurrent finding of severe maternal vitamin D deficiency highlights a potential biological factor deserving further investigation and reinforces the importance of comprehensive clinical assessment at the time of delivery.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no competing interests.

Statement of ethical approval

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was not required for this perspective article. Written informed consent for participation was obtained from the patient.

Statement of informed consent

Written informed consent was obtained from the patient for the publication of anonymized clinical information.

Author Contributions

All authors contributed equally to this article.

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