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Case Report

Pregnancy-associated breast cancer: a case report and literature review

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ABSTRACT

Pregnancy-associated breast cancer (PABC) is a rare, yet significant clinical entity which presents itself during pregnancy or within one year postpartum. This case report and literature review discusses the case of a 33-year-old G1P0 woman diagnosed with PABC at 38 weeks' gestation with an uncomplicated pregnancy and no significant risk factors. Fine needle aspiration revealed a left-sided metaplastic grade 3 invasive ductal carcinoma with heterogeneous mesenchymal differentiation and focal ductal carcinoma in situ, and an uncomplicated nipple-sparing mastectomy was undertaken at three weeks' post-partum. This case report emphasises the need for early diagnosis and the importance of screening for breast cancer during pregnancy, and advocates for a low threshold to screen for PABC in all pregnancies. The literature review also provides updated insights into the presentation, diagnosis, and management of PABC. We explore the diagnostic challenges associated with PABC, including physiological changes in breast tissue during pregnancy, limitations of imaging modalities, and the importance of considering PABC as a differential diagnosis.

Keywords: Breast cancer, Pregnancy, Chemotherapy, PABC

INTRODUCTION

Breast cancer is the most common cancer to affect women globally and poses significant public health and personal challenges. Pregnancy associated breast cancer (PABC) is defined as BC diagnosed during pregnancy or within one year postpartum and affects approximately one in 3,000 pregnancies. In 10% of women diagnosed with BC under the age of 40, the disease is linked to pregnancy, making PABC the second most prevalent pregnancy-associated malignancy following cervical cancer.¹

Pregnancy induces considerable hormonal alterations and structural changes in breast parenchyma, leading to tissue proliferation.² These changes have been postulated to contribute to the pathogenesis of PABC, making it a particularly intricate field of study straddling the domains of oncology and obstetrics.³ Furthermore, younger women diagnosed with breast cancer have been reported to display

distinct biological characteristics and are often subject to more aggressive disease progression.

Historically, PABC has been linked with less favourable outcomes when compared to non-pregnancy-associated breast cancers. This has been largely attributed to diagnosis delays and the unique physiological considerations that can complicate treatment.⁴ However, the literature reveals a spectrum of outcomes, with some studies reporting similar or even improved survival rates in comparison to non-PABC cases. This disparity underscores the need for more in-depth investigation and understanding of PABC. Treatment decisions in PABC are further complicated by the imperative to ensure foetal safety, which can significantly impact therapeutic strategies.⁵ Over the past few decades, an expanding body of literature has sought to navigate these complexities, providing valuable insights into the epidemiology, pathology, diagnosis, management, and prognosis of

PABC. Yet, the landscape of PABC remains riddled with unanswered questions, making it an imperative area of further study.

The frequency of PABC is expected to rise due to women delaying childbirth and a surge in breast cancer incidence, particularly among young women of reproductive age. Therefore, a high clinical suspicion for any expectant or postpartum woman experiencing breast symptoms is crucial to recognising the disease. Here, we discuss the case of a 33-year-old G1P0 woman diagnosed with PABC during her third trimester of pregnancy and the challenges faced in the diagnostic workup and treatment strategies.

CASE REPORT

A 33-year-old primiparous patient discovered a mass in her left breast while antenatally expressing at 35 weeks gestation. She attended her local general practitioner, who requested a breast ultrasound (Figures 1 and 2).

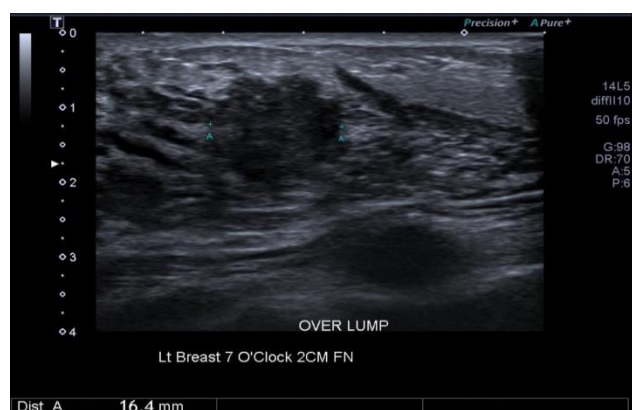


Figure 1: Initial ultrasound of the left breast showing a heterogeneously hypoechoic, ill-defined mass with suggestion of angular margins, measuring 16×19×15 mm, taller than wide and probable internal calcifications.



Figure 2: Doppler image depicting the high vascularity of the same left breast mass.

At 38 weeks gestation, she was diagnosed with mesenchymal metaplastic breast cancer with no axillary lymph node involvement via fine needle aspiration (FNA)

(Figures 3-5). The patient had no relevant past medical history of smoking, IVDU, breast changes pre-pregnancy, sexually transmitted infections, or early menarche. She does not have a family history of cancer, and her pregnancy was otherwise uncomplicated.

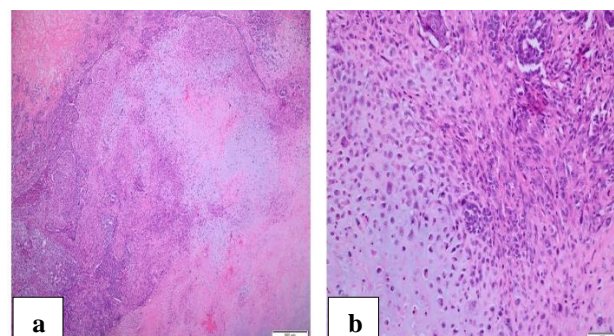


Figure 3: Low and medium power views demonstrate biphasic lesion comprised of both malignant epithelial and myxochondroid elements (a) 4x and (b) 20x.

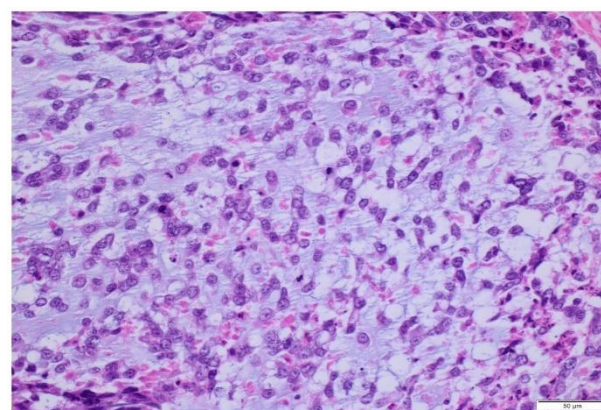


Figure 4: High power view demonstrating mesenchymal differentiation of malignant cells.

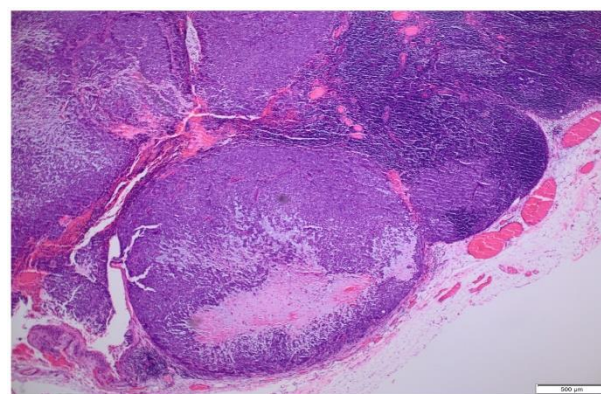


Figure 5: Metastatic carcinoma within lymph node, including myxochondroid component.

Labour was induced at 40 weeks to allow for prompt surgery and minimise risk to baby. Because delivery planning was prioritised, antenatal cancer staging investigations were not performed. Initially the patient

declined early labour induction in favour of a minimal medical intervention childbirth, but the risk to prognosis eventually led the patient to agree to induction with artificial rupture of membranes at 40 weeks without Syntocinon. Following a 9-hour labour she proceeded to a normal vaginal water birth at 40+0 weeks gestation with a second-degree tear requiring sutures and an estimated blood loss of 200ml. She delivered a healthy baby with an appearance, pulse, grimace, activity, and respiration (APGAR) score of 9¹ and 9⁵, and birth weight of 3470 g.

Prior to surgery and after delivery, the patient underwent a computed tomography (CT) chest-abdomen-pelvis and bone scan. The CT confirmed there was no locoregional or distant metastatic disease within the thoracoabdominal region. The bone scan confirmed there was no evidence of osteoblastic skeletal metastasis. She did not have a PET scan.

The patient was scheduled for a nipple-sparing left breast mastectomy with axillary lymph node removal three weeks post-partum. The mother was asked to stop breastfeeding prior to surgery and to use cold packs to minimise the risk of surgical complications such as mastitis and milk fistula formation. By day nine post-partum she was exclusively formula feeding.

At the time of surgery, a breast expander was placed rather than the implant size previously ordered as measurements taken while she was lactating over-estimated their size on the day of surgery. Diathermy was used preferentially over sharp dissection (i.e., scalpel) to accommodate for the increased tissue vascularity related to younger age and postpartum state. Although some milk ducts were present in the breast, the surgery was overall uncomplicated.

Histopathological analysis revealed metaplastic grade 3 invasive ductal carcinoma with heterogeneous mesenchymal differentiation and focal DCIS. The tumour was ER/PR and Her2 negative. Before chemotherapy, the patient was referred to a fertility specialist and opted for stimulation and egg collection. Her chemotherapy regime consisted of doxorubicin cyclophosphamide (DD-AC) followed by carbo paclitaxel and used Zoladex during chemotherapy for ovarian preservation.

DISCUSSION

The increasing incidence of pregnancy-associated breast cancer (PABC) poses significant repercussions for patients, and for obstetricians the main concern is preventing harm to both mother and baby. This case report highlights the rare yet noteworthy clinical phenomenon of PABC presenting at 35 weeks gestation without risk factors, which ultimately led to a diagnosis at 38 weeks. The presentation of PABC late in the patient's pregnancy journey addresses the need for regular screening in pregnant and postpartum patients, given standard breast cancer screening programs do not begin until 50 years of age in most countries.

The absence of risk factors for BC aside from age shines a light on the possible rapid development of PABC during pregnancy in otherwise low-risk women. The average age of PABC onset is 33 years and average gestational age is 21 weeks, however a diagnostic delay ranging from 5-10 months is observed, as compared with 1-4 months in non-pregnant patients.¹ Nonetheless, PABC is only defined until one year following pregnancy, so tumours present in pregnancy which are dismissed by patients could be reclassified incorrectly. This is even more pertinent for women who choose to breastfeed for a longer period. The various masking factors during pregnancy and lactation, including increased volume and density of breasts, and education about self-examinations during pregnancy certainly make the likelihood of PABCs being missed high.

The unique hormonal environment of pregnancy, with oestrogen and progesterone being known mitogens, may contribute to malignancy and incidence of PABC which if gone unnoticed, could enter dormant or slow-growing stages once mitogens normalise following pregnancy, only to remit later. A previous case report found a 27-year-old only brought the lump into conversation due to its fast-growing character, and many patients may shrug off smaller lumps due to pregnancy-related change or may not self-examine at all if not instructed.⁶ Similarly, in this case the tumour was initially discovered by the patient, making it entirely possible PABCs could be more common and missed. Considering 6.6% of new breast cancers are found in women under 40 years of age and older age at first pregnancy is a known risk factor for later cancer breast screening throughout pregnancy and a low threshold for investigating should be advocated for by obstetricians.⁷

Although palpation may be difficult with rapidly growing breasts, this case report and previous studies suggest a standard breast examination should be performed at the first obstetric visit for patients greater than thirty years or other risk factors for cancer, while all patients should be encouraged to self-examine considering younger ages are associated with PABC. If a breast mass is detected and has lasted more than two weeks, a breast ultrasound should be requested, and a fine needle aspirate can be performed if suspicions are confirmed. Reassuringly, approximately 80% of biopsies during pregnancy are benign however in the unlikely case of PABC, investigations should be completed without delay due to its high metastatic potential.⁸ In this case, antenatal staging investigations were not completed, instead opting for prompt delivery, and to confer the smallest radiation exposure to the foetus. Due to the rarity of metaplastic PABC, there is no standard evidence-based systemic therapy regimen, however surgical excision is often first-line. This patient underwent a nipple-sparing left breast mastectomy with axillary lymph node removal three weeks post-partum. Following surgery, the patient was offered DD-AC followed by the carbo paclitaxel, and so the baby continued to be exclusively formula fed. Case-control studies have shown similar rates of survival and chemosensitivity between

pregnant and non-pregnant patients diagnosed with BC when receiving the same standard of care involving surgery and neoadjuvant or adjuvant chemotherapy. In addition, BC treated during the second and third trimesters with either adjuvant or neoadjuvant systemic therapy using 5-fluorouracil, doxorubicin, and cyclophosphamide imparted no significant short-term complications for the children exposed in utero and conferred similar prognostic benefits to non-pregnant patients.⁹ Due to risks to the foetus, including prenatal death, organ malformation, and increased risk of childhood cancer, radiotherapy is a relative contraindication of pregnancy and may only be considered if other adjunct therapies fail.¹⁰ In cases of chemotherapy, patients with PABC may continue to breast feed from the contralateral breast leading up to surgery for psychosocial reasons and attachment but should be withheld until after at least five serum half-lives of the chemotherapeutic agent are excreted from the body.¹⁰

Whilst the survival rate of PABC is similar to non-pregnant patients once matched for age and stage, the diagnosis juxtaposed with the start of a new life stage emphasises the need for this to be considered in treatment guidelines. Therefore, a highly individualised, multidisciplinary approach should be taken in all PABC patients, with consideration of psychosocial implications. In the general management of PABC, surgical intervention can be considered at any stage of pregnancy, while chemotherapy can typically be administered during the second and third trimesters. For diagnoses in the third trimester, a planned term induction is often advisable. Radiotherapy, however, is generally postponed until after childbirth. Importantly, immediate staging investigations should be performed without delay, unless an early delivery is opted for. The surgical approach to breast cancer during pregnancy parallels that of non-pregnant patients, with some additional considerations for lactation. For instance, breastfeeding can continue with the unaffected breast. Nevertheless, the use of radiotherapy and chemotherapy necessitates more intricate considerations due to their potential impacts on both mother and foetus. Thus, every step in managing PABC calls for a fine balance between effectively treating the cancer and ensuring the safety and wellbeing of both mother and baby.

CONCLUSION

This case study showcases the unique presentation of a 33-year-old woman presenting at 35 weeks with a breast mass which ultimately was diagnosed as metaplastic PABC. A delay in BC diagnosis is common in pregnancy and given 10% of women diagnosed with BC are under the age of 40 regular surveillances should be considered for expectant and lactating mothers.

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