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CASE REPORT

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Pregnancy during adjuvant tamoxifen therapy: A case of temporary interruption and postpartum metastatic recurrence

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Abstract

Background: Limited data exist regarding recurrence risk in pregnant women with hormone receptor-positive breast cancer who temporarily discontinue endocrine therapy.

Case presentation: A 37-year-old gravida 4, para 3, presented for antenatal care at 13 weeks' gestation while on adjuvant tamoxifen, which she had taken for two months before conception. Examination revealed a fundal height of 18 weeks and a healed mastectomy scar. Ultrasonography confirmed a dichorionic diamniotic twin pregnancy. Tamoxifen was discontinued, and pregnancy proceeded uneventfully until spontaneous preterm delivery at 34 weeks. Both neonates were clinically normal. Tamoxifen was resumed postpartum; however, 5 months after delivery, the patient developed metastatic recurrence and subsequently succumbed.

Conclusion: Pregnancy during breast cancer is not uncommon and poses complex clinical challenges. A multidisciplinary team is key to optimize maternal and neonatal outcomes.

Keywords: breast cancer, endocrine therapy, metastasis, pregnancy, tamoxifen

Introduction

Breast cancer is among the most common malignancies affecting women, with an estimated prevalence of approximately 34 cases per 100,000 women in Kenya (1). Standard adjuvant treatment for hormone receptor-positive disease typically includes endocrine therapy, such as tamoxifen, a selective estrogen receptor modulator that reduces the risk of recurrence when administered for 5-10 years (2). However, tamoxifen can induce ovulation, leading to unintended pregnancies in women of reproductive age, and its long half-life complicates management when conception occurs unexpectedly. Decisions regarding treatment are further influenced by fertility desires, which may affect disease outcomes (3). Concerns also remain about whether pregnancy itself increases the risk of recurrence with hormone receptor-

positive disease. Retrospective studies, however, have not demonstrated an association between subsequent pregnancy and worse breast cancer outcomes (4). Data from clinical trials suggest that temporarily interrupting endocrine therapy to allow conception does not increase the risk short-term recurrence (5). Additional considerations include the safety of tamoxifen exposure during pregnancy and lactation. Although tamoxifen inhibits lactation by suppressing prolactin secretion, its excretion into breast milk is uncertain, and breastfeeding is generally discouraged (6). Further, case reports and animal studies have reported congenital anomalies after in utero exposure, though long-term pediatric outcome data are limited (7,8). This is a case of a gravida 4 who conceived while on adjuvant tamoxifen, with exposure during first trimester, temporary treatment interruption, preterm delivery of healthy twins, and postpartum metastatic recurrence.

Case presentation

A 37-year-old gravida 4, para 3, was referred to the antenatal clinic at Kenyatta National Hospital (KNH) from the hospital's Cancer Treatment Center (CTC), where she had been under follow-up for breast cancer. She had been on tamoxifen therapy for two months before conceiving unexpectedly. Eighteen months prior to conception, she had been diagnosed with grade 2 invasive ductal carcinoma, positive for estrogen and progesterone receptors and negative for human epidermal growth factor receptor (HER2). She underwent a modified radical mastectomy, and postoperative staging revealed a $T_2N_2M_0$ stage. This was followed by six cycles of adjuvant chemotherapy with doxorubicin, cyclophosphamide, and paclitaxel, completed two months after surgery. Additionally, she received 21 sessions of chest and axillary radiotherapy due to nodal involvement. Hormonal therapy with tamoxifen was initiated one year after diagnosis, with regular follow-up at the CTC. Her pregnancy was discovered during the fifth month of tamoxifen therapy, when she was found to be 13 weeks pregnant.

At the antenatal clinic, gestation was estimated at 12 weeks and 4 days by her last menstrual period, while fundal height corresponded to 18 weeks. Apart from a well-healed right mastectomy scar (**Figure 1**), her general and systemic examinations were unremarkable. Obstetric ultrasound scan confirmed a viable dichorionic diamniotic twin gestation at 13 weeks and 6 days (**Figure 2**). Antenatal laboratory profile results were within normal limits. She was commenced on multinutrient supplements and low-dose aspirin. A multidisciplinary team (MDT) comprising a feto-maternal specialist, medical oncologists, breast surgeons, and gynecologic oncologists reviewed the case and recommended discontinuation of tamoxifen for the remainder of the pregnancy. The patient received counseling on potential risks and management options and consented to the MDT plan.

A fetal anomaly scan at 20 weeks was unremarkable, and antenatal visits were scheduled every two weeks. In addition to the routine care, each visit included a clinical evaluation for symptoms or signs of breast cancer recurrence or metastasis. Apart from mild nausea, early satiety, fatigue, and episodic breathlessness, the pregnancy progressed uneventfully until 34 weeks, when she presented in the second stage of labor. Vaginal delivery of twins was achieved. The first twin was a female, weighing 1900g with Apgar scores of 9 (1 min) and 10 (5 min), and the second twin was a male neonate, weighing 2000g with Apgar scores of 6 (1 min), 7 (5 min), and 8 (10 min). The neonates were exclusively fed infant formula, and the mother resumed tamoxifen therapy soon after delivery.

During postnatal and oncology follow-up, she developed epigastric pain and a productive cough one week postpartum. Examination revealed right basal chest crackles and epigastric tenderness, but no respiratory distress. Laboratory investigations, included complete blood count, renal and liver function tests were unremarkable, except for elevated c-reactive protein at 102 mg/L (refer-

ence range <1 mg/L). The sputum GeneXpert test was negative for tuberculosis. Chest radiography revealed moderate right pleural effusion, confirmed on computed tomography (CT) of the chest, with no other abnormalities. Abdominal and pelvic CT scans were normal.

Thoracentesis attempts resulted in a dry tap, and cardiothoracic surgeons deemed chest tube drainage unnecessary. She was managed with oral amoxicillin-clavulanate 1 g twice daily for one week and omeprazole 40 mg daily for two weeks, with symptom resolution. She remained stable through the puerperium and consented to copper intrauterine device insertion for contraception. Five months postpartum, she presented with respiratory distress. Repeat chest CT revealed a left breast tumor with diffuse skin thickening and chest wall invasion, left axillary lymphadenopathy, right loculated pleural effusion, right pleural-based nodular masses, and hepatic metastases. Tube thoracostomy was performed, but the patient succumbed a few days later. The twins remained healthy, attaining normal developmental milestones.

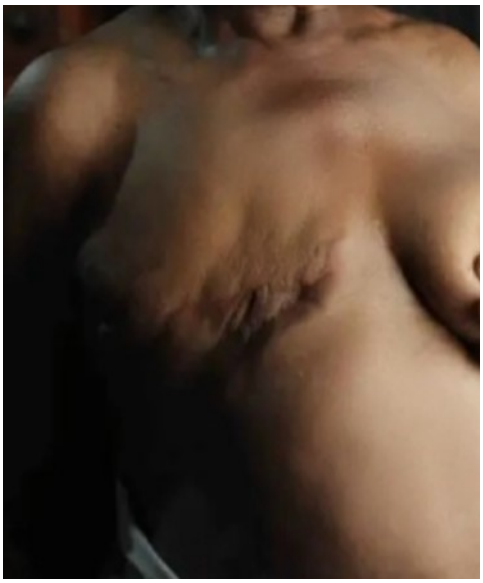

FIGURE 1: RIGHT HEALED MASTECTOMY SCAR

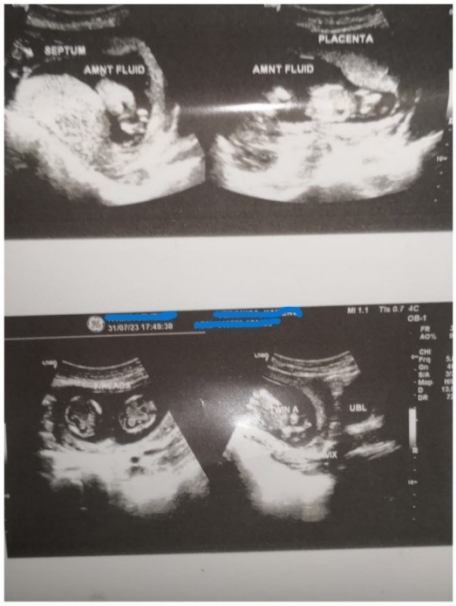

FIGURE 2: EARLY TRIMESTER ULTRASOUND SHOWING TWIN PREGNANCY

Discussion

In patients with hormone receptor-positive early breast cancer, temporary interruption of endocrine therapy to attempt pregnancy has not been associated with significant short-term adverse effects (4). The European Society for Medical Oncology (ESMO) recommends the resumption of endocrine therapy soon after delivery (9). In the POSITIVE trial, the 3-year incidence of breast cancer recurrence after endocrine therapy interruption was 8.9% (95% CI, 6.3-11.6) in the treatment-interruption group compared with 9.2% (95% CI, 7.6-10.8) in the control group, after a median follow-up of 41 months (5). In the present case, there was no evidence of breast cancer recurrence during pregnancy or the puerperium following tamoxifen interruption at 13 weeks of gestation. However, recurrence with distant metastasis occurred five months postpartum, despite prompt resumption of tamoxifen after delivery. As this is a single case, it may not accurately represent the risk or timing of recurrence following temporary discontinuation of tamoxifen.

Live births, both with and without congenital anomalies, have been reported following

tamoxifen exposure before pregnancy, alongside instances of spontaneous abortion and stillbirth (8). Some studies suggest a higher risk of preterm birth among women who conceive within one year of initiating chemotherapy compared to those who conceive later (10). In this case, conception occurred more than a year after chemotherapy, but preterm birth still ensued, likely influenced by the multifetal gestation rather than the timing of conception.

Tamoxifen has documented teratogenic potential (11) and is classified as a pregnancy category D drug by the U.S. Food and Drug Administration (FDA). Guidelines recommend reliable contraception during and for at least two months after discontinuation due to the long half-life of its active metabolite, N-desmethyl tamoxifen (12). ESMO contraindicates tamoxifen use at any stage of pregnancy because of teratogenicity concerns and recommends individualized counseling when inadvertent exposure occurs (8,9). While congenital anomalies have been reported, their overall incidence (2.2% per 365 newborns) remains similar to that in the general population (13). In this case, tamoxifen exposure occurred throughout the first trimester before treatment interruption. Following multidisciplinary discussion and counseling, the patient opted to continue the pregnancy. A 20-week anomaly scan and subsequent neonatal assessments at birth and five months postpartum revealed no overt malformations. Nevertheless, ESMO advises long-term follow-up of such children to monitor behavioral and cognitive development (9).

Given the limited data on the safety of breastfeeding during endocrine therapy, it is recommended that newborns of mothers on tamoxifen receive alternative feeding. The National Comprehensive Cancer Network (NCCN) discourages breastfeeding during endocrine treatment and advocates nonhormonal contraception for women receiving such treatment (6). For those not desiring future fertility, tubal ligation or vasectomy is appropriate, whereas barrier methods or a copper intrauterine device may be used in women who wish to conceive later (6,7). Accordingly, the twins in this case were exclusively formula-fed, and a copper IUD was selected for postpartum contraception.

Conclusion

Pregnancy during breast cancer is not uncommon and poses complex clinical challenges. A multidisciplinary team is key to optimize maternal and neonatal outcomes.

Consent for publication

Informed consent for publication was obtained from the patient.

Conflict of interests

The authors declare no conflicts of interest.

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None

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