Favourable pregnancy outcome following inadvertent exposure to trastuzumab, tamoxifen and radiotherapy in a patient with breast cancer: a case report

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Abstract

Breast cancer is the most common malignancy among women worldwide and often affects those of reproductive age. Treatment typically involves surgery, chemotherapy, radiotherapy, targeted therapy, and endocrine therapy, several of which are contraindicated during pregnancy due to fetal toxicity. We report a rare case of unrecognized pregnancy in a 28-year-old woman receiving adjuvant therapy for breast cancer. Following excisional biopsy showing infiltrating ductal carcinoma, she underwent neoadjuvant chemotherapy, modified radical mastectomy, radiotherapy, and was receiving trastuzumab with tamoxifen. An ultrasound performed for abdominal discomfort revealed a 32-week viable pregnancy. At the time of diagnosis of pregnancy she was taking daily tamoxifen, on maintenance trastuzumab and in retrospect she had received radiotherapy after conception. She later delivered a healthy baby by caesarean section, and both mother and child remain well at two-year follow-up.

Keywords: Breast cancer, pregnancy, trastuzumab, tamoxifen, radiotherapy

Introduction

Breast cancer is the most common malignancy affecting women worldwide and is the second most common malignancy affecting pregnant women.[1] In majority of patients, management of breast cancer requires multimodality treatment including surgery, chemotherapy, radiotherapy, targeted therapy and endocrine therapy. These treatments have potential teratogenic effects so pregnancy during active treatment of breast cancer poses significant clinical and ethical challenges.[2]

Surgery itself does not directly compromise the fetus; however, the use of general anaesthesia may potentially affect fetal well-being. Unintentional exposure of fetus to anti-cancer therapies is considered high risk. Endocrine therapy with tamoxifen has been associated with congenital anomalies and therefore it's use is contraindicated in pregnancy and should be stopped at least 2-6 months before planned pregnancy.[3] Anti-HER2 therapy such as trastuzumab has been reported to cause oligohydramnios, anhydramnios, and fetal renal complications however if pregnancy occurs during trastuzumab therapy then it should be stopped and pregnancy could be continued after proper discussion.[4] Radiotherapy also carries potential risks to the fetus like growth restriction, congenital malformations and neurodevelopmental impairment particularly when the exposure occurs during early exposure. [5]

Current guidelines recommend effective contraception and pregnancy testing in patients receiving systemic therapy for breast cancer.[6] Nevertheless unrecognised pregnancy during treatment may rarely occur as menstrual irregularities develop during chemotherapy or endocrine therapy.

We report an unusual case of an unrecognised third-trimester pregnancy in a patient undergoing adjuvant treatment for breast cancer, who had inadvertent exposure to radiotherapy in first trimester and was receiving maintenance trastuzumab along with daily tamoxifen.

Case report

A 28-year-old woman presented to us after undergoing an excisional biopsy for a right breast lump at another center. Histopathological examination revealed infiltrating ductal carcinoma, grade II. Immunohistochemistry showed estrogen

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receptor (ER) positivity of 95%, progesterone receptor (PR) positivity of 5%, and HER2 3+ and Ki67 of 60%. Staging investigations demonstrated postoperative changes in the breast along with multiple enhancing lymph nodes in the right axilla, the largest measuring 4 cm, and additional nodes in the right internal mammary region.

She subsequently received six cycles of neoadjuvant chemotherapy with the TCH regimen consisting of docetaxel, carboplatin, and trastuzumab. Following completion of chemotherapy, she underwent a modified radical mastectomy. Final histopathological examination revealed a pathological complete response in the breast with residual nodal disease, staged as ypT0N2a (4/16). Postoperatively, she received radiotherapy (40Gy/15# followed by 10Gy/15# electron boost to IMN region) using three-dimensional conformal radiotherapy (3D-CRT). Adjuvant therapy with trastuzumab every three weeks was continued, and endocrine therapy with tamoxifen was initiated.

She presented to the surgical outpatient department with an ultrasound report performed at a local clinic at her request for abdominal discomfort, which revealed a live fetus weighing approximately 1954 gm with an estimated gestational age of 32 weeks. This was the first time that the patient and her family became aware of the pregnancy. She was subsequently referred to maternity center, where she delivered a healthy baby girl weighing 2.1kg by caesarean section on same day. At the time of diagnosis of pregnancy, she had received her 16th cycle of trastuzumab one week earlier and was on daily tamoxifen. In retrospect, she had also received radiotherapy after conception. She was advised not to breast feed baby and tamoxifen was resumed after one month.

Both mother and child have remained well on follow-up. At two years after delivery, the child has demonstrated normal growth and developmental milestones. The lady is taking tamoxifen and continues regular oncological follow-up without evidence of disease recurrence.

Discussion

Breast cancer is the most common malignancy affecting women worldwide and a significant proportion of patients are diagnosed during their reproductive years. While treatment for pregnant patients should adhere to treatment guidelines for non-pregnant patients, there exists specific considerations concerning staging, oncological treatment & obstetrical care. [7] Most systemic therapies used in breast cancer are potentially teratogenic and are therefore contraindicated during pregnancy.

In our patient, the pregnancy was diagnosed at 32 weeks of gestation after an ultrasound examination for abdominal discomfort which is very unusual presentation of pregnancy. Unrecognised pregnancy also referred to as cryptic pregnancy is a relatively rare event. Such situations may occur due to irregular menstruation, obesity, lack of typical pregnancy symptoms, or misattribution of symptoms. In patients undergoing cancer therapy, treatment-related amenorrhea may further contribute to delayed recognition of pregnancy, which is one of the factors in our case as menstruation has not resumed after neoadjuvant chemotherapy. It has been estimated that approximately 1 in 475 pregnancies remain undiagnosed until 20 weeks of gestation while diagnosis only in third trimester occurs in roughly 450-500 pregnancies and about 1 in 2500 pregnancies are not recognised until the onset of labour. [8,9]

Tamoxifen exposure during pregnancy has been associated with fetal malformations including craniofacial anomalies and genital abnormalities.[10] Our patient was taking tamoxifen till the day of diagnosis of pregnancy. Tamoxifen persists in the body for several weeks and may have terotogenic effects on the developing fetus if conception occurs soon after discontinuation, this is the reason it is advised to discontinue tamoxifen and allow a washout period ranging from 2 to 6 months before attempting conception. [11]their reproductive outcomes, and maternal safety were assessed. Pooled relative risks, odds ratios (ORs We advised not to breast fed the baby as it is recommended to wait for about 2 months for drug washout before initiating breast feeding. Tamoxifen was started after one month of delivery of baby.

Trastuzumab administration during pregnancy has been associated with oligohydramnios or anhydromnios, believed to result from inhibition of

epidermal growth factor receptor signalling in the fetal kidney.[4] Our patient has received trastuzumab throughout the entire pregnancy period, with the last dose (16th dose) administered one week prior to the diagnosis of pregnancy. The subsequent remaining last dose was not administered as more than one month had already elapsed by the time she presented to us after delivery.

Radiotherapy during pregnancy also raises concerns regarding fetal exposure to ionising radiation. However, when radiotherapy is delivered to the breast the scattered radiation dose reaching the uterus is usually minimal, particularly in early gestation, which might have happened to our patient. In retrospect, she had received radiotherapy after conception.

This case report highlights the importance of careful counselling regarding contraception in women of reproductive age group undergoing cancer treatment. At the same time, this report contributes to the limited body of literature suggesting that favourable outcomes may occur despite such exposures however such outcomes cannot be generalized, and caution remains essential.

Conclusion

Inadvertent exposure to trastuzumab, tamoxifen, and breast radiotherapy during pregnancy is rare. Although adverse fetal effects have been reported, our case demonstrates that favourable maternal and fetal outcomes may occasionally occur. Nevertheless, strict contraception counselling and routine pregnancy testing are essential in women receiving systemic therapy for breast cancer.

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