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Tamoxifen Use in Pregnancy

Remya Aryad*, Edmund Gomez, Emeil Kamel

Blacktown Hospital, NSW, Australia

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***Corresponding author:** Remya Aryad. Blacktown Hospital, NSW, Australia

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ABSTRACT

Tamoxifen is a teratogenic drug that is not used in pregnancy. But women can accidentally conceive on tamoxifen, if no proper contraception is used during its therapy. We present the cases of two young women who were on tamoxifen therapy for treatment of breast cancer, conceived and the pregnancy diagnosed at 20 weeks on a CT scan done surveillance and disease staging. These two women took tamoxifen in the first trimester and continued until pregnancy was diagnosed in the second trimester. Both had uncomplicated pregnancies, with no reported congenital abnormalities or other disorders for the babies.

Keywords: Tamoxifen; Drug; Pregnancy

BACKGROUND

Tamoxifen is a well-established and effective treatment for estrogen receptor-positive breast cancer 1,[1] especially in pre-menopausal women and it reduces the death rate from the disease.[2] Given that there is an increase in the incidence of breast cancer in under 50 age groups,[3] more and more women in the reproductive age group are taking tamoxifen and accidental pregnancies in these women can expose the fetus to the risk of exposure to tamoxifen. Tamoxifen is also known to induce ovulation[4] and this makes the women more fertile, especially at the beginning of treatment. Here we discuss two cases of women who had unplanned pregnancies while on tamoxifen therapy for breast cancer. Both had uncomplicated pregnancies and delivered healthy children with no reported congenital abnormalities.

CASE PRESENTATION

Case 1: A nulliparous, 33-year-old female, was diagnosed with grade 2 ductal carcinoma of left breast with metastatic disease. She was treated with bilateral mastectomy and axillary clearance and also underwent spinal surgery for metastatic bone disease. The tumor was oestrogen receptor positive and she was given tamoxifen and Goserelin. She took tamoxifen for almost a year and was amenorrhoeic while on tamoxifen. She was not using any contraception while on tamoxifen. A CT of the spine done for suspicion of recurrence of lesion diagnosed a

pregnancy at 20 weeks. Tamoxifen and Goserelin were both ceased following confirmation of pregnancy. The pregnancy progressed well and she underwent an elective cesarean section with bilateral salpingo oophorectomy at 33 weeks to continue treatment for her pelvic metastasis. A male baby of weight 2.7 kg was born without any anomalies and only had supportive treatment in the NICU for problems associated with prematurity.

Case 2: A 40-year-old woman, GxPx was diagnosed with grade 2 invasive lobular carcinoma in 2015. A left mastectomy was performed and she underwent adjuvant chemoradiation. The tumour was ER and PR receptor positive and she was commenced on tamoxifen after a year. She had been on tamoxifen for 4 years and was amenorrhoeic while on tamoxifen. She had 2 normal vaginal deliveries 10 years and 7 years ago with no complications. She had a CT Abdo-pelvis for chronic abdominal pain which noticed a fetus of 19 weeks' gestation. Morphology scan revealed no morphological abnormalities. NIPT was low risk. Tamoxifen ceased at 20 weeks and her pregnancy progressed without any complications. She went into spontaneous labor at 39 weeks 4 days and delivered a 3 kg female baby with Apgar's 9 at 1 minute and at 5 minutes. Baby was breastfed, discharged home with mother on day 3. The baby had normal developmental milestones and no reported abnormalities at 1 year of age.

OUTCOME AND FOLLOW-UP

DISCUSSION

The two cases discussed here have similar histories, where both patients were started on tamoxifen for oestrogen receptor positive breast cancer and were not given contraception advice. The patients were not aware of the ovulation induction property of tamoxifen and increased risk of pregnancy with its use. They were diagnosed to be pregnant at 20 weeks, on Computerised tomography performed for disease surveillance. Tamoxifen was ceased in both cases and pregnancy continued after proper counselling and tertiary level ultrasound scans with maternal fetal medicine specialist to rule out structural abnormalities. Reassuringly, both babies were delivered without any structural abnormalities.

Studies in animals have demonstrated adverse effects of tamoxifen on the fetus and fetal loss. Epithelial changes similar to those seen after administration of diethylstilbestrol (DES) or clomiphene citrate have been reported in mice and rats exposed to tamoxifen.[5] There are several case reports on babies born of mothers using tamoxifen in pregnancy. The Astra Zeneca database records showed 11 babies with congenital malformations of 44 live births.[6] In addition, there were 12 spontaneous abortions, 17 terminations of pregnancy without known fetal defects, six terminations of pregnancy with fetal defects, one stillbirth without fetal defects, two stillbirths with fetal defects, and 57 unknown outcomes. The birth defects reported are - congenital hand malformations, vaginal adenoma at 2.5 years, a girl with XXX chromosomes and a phallic like clitoris and huge labia, idiopathic chylothorax, Goldenhar's syndrome, cleft palate, trisomy 21, small degree of labial fusion, craniofacial defects, clitoral hypertrophy. A case report by Tiwari reported ambiguous genitalia.[7] There was also a report of Pierre Robin sequence associated with first trimester fetal tamoxifen exposure.[8] A review of 238 cases of tamoxifen use during pregnancy were reported

by Schuurman etal.[9] Of the 167 pregnancies with known outcome, 21 were complicated by an abnormal fetal development. The malformations described were non-specific and the majority of cases concerned healthy infants despite exposure to tamoxifen. Their research showed an increased risk of fetal abnormalities when taking tamoxifen during pregnancy (12.6% in contrast to 3.9% in the general population), but the evidence is limited and no causal relationship could be established.

On the other hand, Clark published an abstract in The Lancet about 85 women who became pregnant while receiving prophylactic tamoxifen as part of a trial in healthy women at high risk for breast cancer. No fetal abnormalities were observed but the author did not indicate the duration of tamoxifen treatment during pregnancy.[10]

LEARNING POINTS

The two cases reported had been on tamoxifen in the first trimester till the end of 20 weeks. These patients were not aware of the increased risk of pregnancy with tamoxifen and were not offered any contraception.

- Tamoxifen should be considered a teratogen, even though no causal relationship could be established, as abnormalities are reported with tamoxifen use.
- Tamoxifen is contraindicated during pregnancy and the use of non-hormonal contraception is recommended during tamoxifen treatment and for 2 months after discontinuing treatment, due to the extended half-life of tamoxifen and one of its metabolites.[11]
- Oncologists who prescribe tamoxifen should be aware of this effect of tamoxifen on fertility and should provide counselling regarding this.
- Care for women who conceive while using tamoxifen should be individualised, taking in to consideration, gestational age, fetal ultrasound findings, disease stage and patient wishes.
- The long term effects of children exposed to tamoxifen in utero remain uncertain due to the small patient numbers.

REFERENCES

1. Cuzick J, Baum M. Tamoxifen and contralateral breast cancer. The Lancet. 1985;326(8449):282.
2. Tamoxifen for early breast cancer: an overview of the randomised trials. Early Breast Cancer Trialists' Collaborative Group. Lancet. 1998;351(9114):1451–67.
3. Lima SM, Kehm RD, Terry MB. Global breast cancer incidence and mortality trends by region, age-groups, and fertility patterns. EClinicalMedicine. 2021;38:100985.
4. Jie L, Li D, Yang C, Haiying Z. Tamoxifen versus clomiphene citrate for ovulation induction in infertile women. Eur J Obstet Gynecol Reprod Biol. 2018;228:57-64.
5. Cunha GR, Taguchi O, Namikawa R, Nishizuka Y, Robboy SJ. Teratogenic effects of clomiphene, tamoxifen, and diethylstilbestrol on the developing human female genital tract. Hum Pathol. 1987;18(11):1132-43.

6. Braems G, Denys H, de Wever O, Cocquyt V, van den Broecke R. Use of Tamoxifen Before and During Pregnancy. Oncologist. 2011;16(11):1547-51.
7. Tewari K, Bonebrake RG, Asrat T, Shanberg AM. Ambiguous genitalia in infant exposed to tamoxifen in utero. Lancet. 1997;350(9072):183.
8. Berger JC, Clericuzio CL. Pierre Robin sequence associated with first trimester fetal tamoxifen exposure. Am J Med Genet A. 2008;146A(16):2141-4.
9. Schuurman TN, Witteveen PO, van der Wall E, Passier JLM, Huitema ADR, Amant F, et al. Tamoxifen and pregnancy: an absolute contraindication?. Breast Cancer Res Treat. 2019;175(1):17-25.
10. Clark S. Prophylactic tamoxifen. The Lancet. 1993;342(8864):168.
11. Barthelmes L, Gateley CA. Tamoxifen and pregnancy. Breast. 2004;13(6):446-51.