Neonatal Loss Secondary to Third Trimester Chemotherapy for Maternal Breast Cancer

Özgür ÖZYÜNCÜ[1], Işın ÜREYEN[1], Sadettin KILIÇKAP[2], Yusuf Alper KILIÇ[3], Sezcan MÜMÜŞOĞLU[1], Sinan BEKSAÇ[1]

Ankara, Turkey

Breast cancer is the most common cancer among women with a lifetime risk of 11%. Pregnancy-associated breast cancer is defined as cancer diagnosed during pregnancy or up to 1 year post partum. Surgery is the definitive treatment for pregnancy-associated breast cancer. For node-positive patients or node-negative patients with a tumor greater than 1 cm, a 4 to 6 month course of chemotherapy is the standard of care. Provided that chemotherapy is not used in the first trimester, it appears to be relatively safe.

A forty-two year old pregnant woman in the third trimester presented with an advanced breast cancer. Since she had an advanced stage cancer and since she was in the third trimester, she was decided to be treated with chemotherapy. After three weeks, an emergent cesarean section was performed because the fetus was in acute distress. On the 20th day, the baby died because of cardiopulmonary arrest. The cause of the death was concluded as perinatal hypoxia secondary to chemotherapy.

Even though chemotherapy is shown to be safe during the second and third trimester in many clinical trials, each case should be handled separately since the assumption of safety may differ in each case. These pregnants should be observed closer

Key Words: Pregnancy, Breast cancer, Chemotherapy

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Introduction

Breast cancer is the most common cancer among women with a lifetime risk of 11% (1 in 9)[1] and is the second most common malignancy in pregnancy after cervical cancer. Breast cancer in pregnancy is expected to be increasingly common as women delay childbearing until later in life.[2]

Pregnancy-associated breast cancer is mostly defined as the one that is diagnosed during pregnancy or up to 1 year post partum.[3] If survival is matched for grade and stage among non-pregnant controls, the survival seems to be equivalent.[4] Breast cancer diagnosed during pregnancy is usually associated with worse prognosis due to delay in diagnosis and treatment.[5]

Hacettepe University Faculty of Medicine, [1]Department of Obstetrics and Gynecology, [2]Department of Medical Oncology, [3]Department of General Surgery, Ankara

Address of Correspondence: *Özgür Özyüncü*
Hacettepe University Faculty of Medicine Department of Obstetrics and Gynecology Maternal Fetal Medicine and Perinatology Sihhiye, Ankara
ozyuncu@hacettepe.edu.tr

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Ultrasonography is the first imaging choice for the pregnant woman and can distinguish between cystic and solid lesions in 97% of patients. Mammography during pregnancy is safe but has a limited role with a high false-negative rate during pregnancy owing to increased density of the breast.[6]

In general, biopsy is the "gold standard" for diagnosis of breast cancer during pregnancy. Breast cancers in pregnant women are histologically similar to those in non-pregnant women. About 75% to 90% of tumors in both groups are ductal carcinomas.[7]

There is no evidence that termination of pregnancy after diagnosis of breast cancer is necessary to improve prognosis.

Surgery is the definitive treatment for pregnancy-associated breast cancer. Mastectomy and axillary dissection are traditionally considered as the best choice for stage I or II and some stage III tumors.[8] For node-positive patients or node-negative patients with a tumor greater than 1 cm, a 4 to 6 month course of chemotherapy is the standard of care.

Provided that chemotherapy is not used in the first trimester, it appears to be relatively safe for subsequent use even though all chemotherapy agents used in the treatment of breast cancer are pregnancy category D.[9] Some of the expected complications included preterm delivery, transient

tachypnea of the newborn, low birth weight, hyaline membrane disease, and transient leucopenia[10] Since the newborn's liver and kidneys cannot metabolize or excrete chemotherapeutic drugs quickly, it may be wise to avoid or reduce chemotherapy for 1 month before delivery.[11]

Radiation therapy generally is not advised because of teratogenicity, and induction of childhood malignancies and hematological disorders.

We report a case of a pregnant woman in the third trimester presenting with an advanced breast cancer.

Case Report

A forty-two year old pregnant woman in the third trimester admitted with an advanced breast cancer. Her breast biopsy revealed grade II invasive ductal carcinoma (ER(-), PR(-)). She applied to Hacettepe Hospital when she was on the 29th week of gestation, two weeks after diagnosis.

When she was hospitalized, fetal biometry was in normal range and fetal well-being tests were normal. Since she had an advanced stage cancer in the third trimester, chemotherapy and delivery after achievement of pulmonary maturity was planned. Two weeks after the first course of chemotherapy (cyclophosphamide (600mg/m^2/day+adriamisin 60mg/m^2/day) fetal well-being tests start to be non-reassuring. At 33weeks of gestation, cesarean delivery was performed due to acute fetal distress. During the cesarean section, meconium was noticed. Fetal measurements were appropriate for gestational age and cord blood ph was 7.103.

On the 20th day, the baby died from cardiopulmonary arrest. During this time meconium aspiration syndrome, lactic acidosis and pancytopenia developed in the neonate. Necrotizing Enterocolitis, sepsis and mitochondrial depletion were suspected. The cause of death was concluded as perinatal hypoxia secondary to chemotherapy.

Discussion

For lymph node positive patients or lymph node negative patients, who have tumor greater than one centimeter, chemotherapy is the standard of care.[13]

All chemotherapeutic agents used during the treatment of breast cancer in pregnancy, are all classified into category D. [9] Complications, which are seen after chemotherapy in utero, frequently consist of IUGR, preterm delivery, low birth weight or transient leucopenia.[10] Teratogenic risk highly depends on the time of application. Fetal malformations occur with an instance of 14-19% depending on the chemotherapeutic agents when administered in the first trimester. The frequency drops to 1-3% thereafter.[14] In the second and third trimester, the use of chemotherapy does not seem to increase the risk of fetal malformations.

A study reports 57 women with pregnancy associated breast cancer that were treated with FAC chemotherapy in an adjuvant or neo-adjuvant setting.[12] Infants showed no significant short term complications when exposed to chemotherapy in-utero in the second and third trimester. In the neonatal period, 10% required mechanical ventilator, and there was one case of hemorrhage going along with thrombocytopenia and neutropenia.[12]

In another trial, fluorouracil, cyclophosphamide, and doxorubicin were administered to 24 pregnant women, who had breast cancer and were in the second and third trimester. None of the infants had birth defects. Complications were preterm delivery, transient tachypnea of the newborn transient leucopenia and low birth weight.[10]

Long term affects of chemotherapy especially on the fertility and the cardiac functions of the off-springs are still questionable.

In our case, the patient was treated with CA chemotherapy in the 31th week of gestation but the baby died on the 20th day of delivery because of the intrauterine hypoxia secondary to chemotherapy. Even though chemotherapy is accepted as safe during the second and third trimester, each case should be handled separately since the assumption of safety may differ in each case.

Maternal Meme Kanseri Nedeniyle Üçüncü Trimesterde Verilen Kemoterapiye Bağlı Neonatal Kayıp

Meme kanseri kadınlarda en sık görülen kanserdir ve hayat boyu riski %11'dir. Gebelikle ilişkili meme kanseri genellikle gebelikte veya postpartum 1 yılda tanı konulan meme kanseri olarak tanımlanır. Gebelikle ilişkili meme kanserinin kesin tedavisi cerrahidir. Lenf nodu tutulumu pozitif olan veya tümörü 1 cm'nin üstünde olan hastalarda standart tedavi 4-6 aylık dönemde verilen kemoterapidir. Kemoterapi, ilk trimester verilmediği takdirde göreceli olarak güvenli kabul edilir.

42 yaşında, gebeliğinin 3. trimesterinde olan hasta ilerlemiş meme kanseri nedeniyle başvurdu. Meme kanseri ilerlemiş olduğu ve gebeliğinin 3. trimesterinde olduğu için kemoterapi kararı alındı. Kemoterapiyi aldıktan üç hafta sonra hasta akut fetal distress nedeniyle acil sezeryana alındı. Bebek yirmi günlükken kardiopulmoner arrest nedeniyle kaybedildi. Ölüm nedeninin kemoterapiye sekonder gelişen perinatal hipoksi olduğu Kabul edildi.

Birçok klinik çalışmada 2. ve 3. trimesterde verilen kemoterapinin güvenli olduğu gösterilmiş olsa da her vaka kendi içinde değerlendirilmeli ve bu gebeler daha yakın izlenmeli.

Anahtar Kelimeler: Gebelik, Meme kanseri, Kemoterapi

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