

CLINICAL VIGNETTE

Management of Breast Cancer During Pregnancy

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Case Report

A 37-year-old patient, 23 weeks pregnant, presented for evaluation of a right breast mass. Initially thought to be due to breast engorgement from pregnancy, ultrasound evaluation revealed a right breast mass measuring 2cm with several suspicious axillary lymph nodes. Biopsy revealed poorly differentiated invasive ductal carcinoma with focal squamous metaplasia, grade 3, Estrogen Receptor (ER) very weakly positive at 13%, Progesterone Receptor (PR) negative, human epidermal growth factor receptor (HER2) negative, and Ki67 88%. One lymph node was sampled and was positive for involvement. Genetic testing was positive for a deleterious mutation in the *BRCA2* gene.

Staging evaluation with bilateral mammogram, chest x-ray, lumbar/thoracic MRI without contrast, and liver ultrasound was negative for metastatic disease. The right breast mass measured 4.7cm by mammogram. Given aggressive locally advanced almost triple negative breast cancer, she was started on neoadjuvant chemotherapy, while continuing the pregnancy, with Doxorubicin and Cyclophosphamide (AC) every three weeks. She received two cycles, but the breast mass did not show clinical improvement. Repeat ultrasound showed increase in size of the mass and number of suspicious lymph nodes.

Given inadequate response to chemotherapy, patient was taken to surgery and underwent a right side modified radical mastectomy with axillary lymph node dissection. Pathology showed a 9.8 x 7.5 x 5.5 cm invasive carcinoma with 22 out of 22 sampled lymph nodes positive. Given continued pregnancy, she did not receive radiation therapy at that time.

She developed new headaches a week after her surgery at 31 weeks gestation. MRI could not be performed with contrast given pregnancy, and one without contrast was normal. She underwent lumbar puncture procedure and cytology returned positive for adenocarcinoma of breast primary. Decision was made in consultation with obstetrics and maternal fetal medicine to deliver the baby at this time to start central nervous system directed treatment for the mother.

Discussion

Pregnancy associated breast cancer occurs in about 1 in 1,000 pregnancies.¹ Up to 3% of all breast cancers are diagnosed in pregnant women.¹ Diagnosis and staging require special considerations. Mammography can be done with shielding of the abdomen to reduce intrauterine exposure. It is of lower sensitivity, however, due to breast changes and

increased density during pregnancy. Breast ultrasound on the other hand is the diagnostic imaging of choice followed by biopsy of any suspicious lesions. Breast MRI can be done safely, but its utility without contrast is questionable. The use of gadolinium-based contrast enhancement during pregnancy is controversial as it can cross the placenta. Gadolinium agents have been found to be teratogenic at high and repeated dosage in animal models.² The only prospective study evaluating the effect of antepartum gadolinium administration reported no adverse perinatal or neonatal outcomes among 26 pregnant women who received gadolinium in the first trimester,³ but given theoretical concern and animal data, use should be limited to situations in which the benefits clearly outweigh the possible risks.⁴ Therefore once cancer diagnosis is confirmed, patients can be safely staged with a chest x-ray (with abdominal shielding), abdominal ultrasound to evaluate the liver for metastatic disease, and possibly MRI without contrast of the spine to rule out bone metastatic disease.

Therapy for breast cancer should not be withheld during pregnancy and should conform as closely as possible to standardized protocols for patients without pregnancy. While chemotherapy should be avoided in the first trimester due to high potential for teratogenicity ranging from 10-20%, during later trimesters various chemotherapy agents can be given safely with risk of fetal malformation down to 1.3%.¹ Anthracyclines are thought to be safe and so are probably taxanes but have less data.¹ Cyclophosphamide and 5-FU are also thought to be safe based on the largest prospective series done at Mayo clinic.⁵ Hormonal therapy is to be avoided and anti-HER2 therapy is contraindicated due to known increased risk of renal toxicity.⁶ External beam radiation necessary for the completion of breast conservation is contraindicated during pregnancy because of the risks associated with fetal exposure to radiation but can usually be postponed safely to after delivery.⁶ Termination of pregnancy is not routinely recommended as it does not improve survival.¹ Various cohort studies of women exposed to chemotherapy after the first trimester have showed a lower birthweight to be most strongly associated with adverse effects.⁷ Therefore, childbirth at full term should be attempted if safe to minimize risk of adverse events.

The patient presented here received chemotherapy during pregnancy but was induced early due to urgent need for intrathecal chemotherapy and radiation therapy that could not be done during pregnancy. A healthy baby girl was delivered at 32 weeks gestation after induction. Complete staging was performed after delivery with whole body PET and brain and

spine MRI. She was found to have leptomeningeal disease throughout the brain and spine, but there was no evidence of disease elsewhere. Patient subsequently received intrathecal methotrexate, radiation therapy, and intrathecal cytarabine sequentially. She was placed on concurrent oral medication, Olaparib, for systemic therapy given BRCA positivity and possible benefit of this medication in patients with this mutation. She achieved a brief remission and improvement in symptoms of nausea and headache. Unfortunately, she had progression of disease and multifocal stroke and was placed on comfort care. She died three months after delivery, while on inpatient hospice. This was five months from time of diagnosis.

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