Diagnostic and Treatment Considerations When Newly Diagnosed Breast Cancer Coincides With Pregnancy: A Case Report and Review of Literature

Lauren Nye, MD; Timothy K. Huyck, MD; and William J. Gradishar, MD

Breast cancer is the most common malignancy associated with pregnancy and is a rare but well-recognized complication. A California registry study showed an incidence of 1.3 breast cancers diagnosed per 10,000 live births. It is hypothesized that as more women continue to delay childbearing, the incidence of breast cancer in pregnancy will increase. Because of the lack of clinical experience with breast cancer in the setting of pregnancy, given its relative infrequency, many patients and physicians believe the diagnosis puts the life of the mother at odds with that of the fetus, but available data suggest that termination of the pregnancy does not improve the outcome for pregnant women with breast cancer. Often diagnosis is delayed because neither patient nor physician suspects malignancy. This report presents a recent case of a young primigravid woman with a newly appreciated breast mass seen at Northwestern University Feinberg School of Medicine as a means of discussing diagnostic considerations, therapeutic options, and supportive care available to the practitioner when managing a pregnant patient with breast cancer. (JNCCN 2012;10:145–148)

Case Report

A 28-year-old primigravid woman at 21 weeks' gestation with a medical history significant for nephrolithiasis, migraines, and irritable bowel syndrome presented with a self-detected right-sided breast mass in the upper outer quadrant. Her only medication was a daily prenatal vitamin. Family history was positive for breast cancer in a maternal grandmother, who was diagnosed...
and treated at 55 years of age. Review of systems was positive for intermittent headaches consistent with previous self-limiting migraines and occasional nausea without emesis, which had been diminishing in frequency since she entered her second trimester. Physical examination was notable for a 2.0 × 3.0 cm irregular breast mass that was firm and located at the 12:30 position, approximately 3 cm from the nipple. No skin or nipple changes were apparent, nor was any evidence present of axillary lymphadenopathy. The remaining examination showed a gravid uterus but was otherwise unremarkable. Right breast ultrasound was ordered.

Ultrasound results showed an irregularly shaped 2.0 × 2.8 × 3.0 cm mass at the 1 o’clock position. The right axilla was also scanned with ultrasound, which showed an enlarged lymph node measuring 1.6 × 2.3 cm with a markedly thickened cortex. This was followed by ultrasound-guided core biopsies of the breast mass and right axillary lymph node. Pathology showed a grade 3 invasive ductal carcinoma of the right breast. Hormonal studies showed a tumor staining positive for estrogen receptors (70%) and progesterone receptors (80%). Her-2/neu was negative at 0%. Ki-67 was 60%. Axillary lymph node biopsy was positive for metastatic carcinoma consistent with the patient’s primary invasive ductal carcinoma of the breast. Given the evidence of nodal involvement, a 2-view chest radiograph with abdominal shielding and an ultrasound of the liver were obtained, which did not suggest distant metastases.

Treatment options, including mastectomy, breast-conserving therapy with axillary staging, and neoadjuvant chemotherapy, were discussed extensively with the patient. Throughout the discussion, the patient clearly stated her goals of continuing the pregnancy. Her physicians did not encourage termination of the pregnancy, because termination was not imperative to her treatment and has not been shown to improve patient outcomes. Given the clinical stage of disease (IIb; T2, N1, Mx; invasive ductal carcinoma), she was offered neoadjuvant therapy with doxorubicin and cyclophosphamide given every 3 weeks for 4 cycles, with the last treatment cycle planned for before 34 weeks’ gestational age to allow for blood count recovery before delivery. After delivery, the patient will be offered paclitaxel therapy every 2 weeks for 4 doses followed by surgical management. Both breast-conserving therapy and mastectomy were discussed with patient. Genetic testing was ordered because of her young age at diagnosis, even in the absence of strong family history of breast cancer. Adjuvant endocrine therapy was recommended after delivery and completion of all chemotherapy.

**Discussion**

Multimodality care is of utmost importance in managing pregnant patients with breast cancer. Teamwork is required and many subspecialists should be involved in the care of the patient, including an obstetrician, perinatologist, medical oncologist, surgical oncologist, and radiation oncologist. Depending on the clinical situation, clinical geneticists and ethicists, pastoral care, and social workers may be needed to provide support. The various specialists should be involved early in the care of the patient to assure proper timing of necessary assessments and interventions.

Evaluation of the pregnant patient with a breast mass concerning for malignancy should include a physical examination, with particular attention to regional lymph nodes. Mammogram of the breast with abdominal shielding in the setting of pregnancy can be performed safely and with greater than 80% accuracy. Ultrasound is safely used in pregnant patients and can help assess regional lymph nodes to determine extent of disease; it is also useful in providing assistance in obtaining biopsy. Ultrasound has been reported to be abnormal in up to 100% of breast cancers occurring during pregnancy. Biopsy of all lesions concerning for malignancy should be performed, and a core biopsy is preferred to a fine needle aspiration to provide sufficient tissue available for hormone receptor and HER2 analyses.

Staging of the pregnant patient is guided largely by clinical evaluation and presence or absence of symptoms suggesting metastases. In patients with biopsy-proven malignancy who are clinically node-negative, workup consisting of a 2-view chest radiograph with abdominal shielding and laboratory evaluation, including liver function analysis, assessment of renal function, and a complete blood cell count with differential, is sufficient. In patients with node-positive disease, a primary tumor larger than 5.0 cm, or symptoms concerning for metastases, a metastatic workup is indicated. This can include a 2-view chest radiograph with abdominal shielding, an ultrasound of the liver, and consideration of a noncontrast MRI of the brain and thoracic and lumbosacral spine in patients whose clini-
cal presentation suggests metastatic disease to these sites. Bone scans and CT are relatively contraindicated in pregnancy because of teratogenic levels of radiation exposure to the fetus, however, the decisions to obtain these tests must be made on an individual basis.

The role of sentinel lymph node biopsy remains controversial given the limited available data regarding safety to the fetus during pregnancy. Several studies performed in nonpregnant women used standard internal dose calculators to estimate what the fetal radiation dose would be in a pregnant woman, and the results show negligible doses. Few reports of retrospective studies with limited sample size (<10 patients each) have shown no adverse events to the fetus in pregnant women who underwent sentinel lymph node biopsy with Tc-99m sulfur colloid. These women went on to have full-term deliveries without any fetal malformations (excluding one patient who electively terminated pregnancy in the first trimester). The risks and benefits of sentinel lymph node biopsy should be discussed with the patient. Blue dyes should be avoided, because they have not been tested in pregnant animal models or humans.

Obstetrics and perinatology will play a pivotal role in assessment of the pregnancy and its associated risks. Estimation of the delivery date will help in planning systemic chemotherapy and will also assure optimal timing of surgical intervention if it is to be undertaken in the postpartum setting. Documentation of fetal growth and development is recommended before each round of systemic chemotherapy. Patients will need to be counseled regarding the potential effects of chemotherapy on the fetus, and a discussion concerning maintaining or terminating the pregnancy is necessary. Termination of pregnancy has not been shown to improve survival in patients diagnosed with breast cancer during pregnancy.

Minimal prospective data are available on the use of chemotherapy in pregnancy; however, studies have consistently shown that chemotherapy is contraindicated in the first trimester because of increased incidence of spontaneous abortions, fetal malformations, and death. In a single-arm prospective clinical trial conducted at MD Anderson Cancer Center, 57 pregnant women with breast cancer received FAC (5-fluorouracil [5-FU], doxorubicin, and cyclophosphamide) starting in their second or third trimester and continuing every 21 to 28 days until gestational age of 35 weeks, with relative safety to both mother and fetus. A case study review by Cardonick et al. included 72 patients with breast cancer exposed to chemotherapy during pregnancy and supported the safety of 5-FU, cyclophosphamide, and doxorubicin after the first trimester. Per the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer, safety data are insufficient to recommend the use of taxanes during pregnancy (to view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org). Further assessment of clinical outcomes and pharmacokinetics with taxanes has been recommended. Current recommendations for adjuvant or neoadjuvant therapy in pregnancy include the use of 5-FU, cyclophosphamide, and doxorubicin. Dose-dense chemotherapy is typically not given during pregnancy because of the need for administration of granulocyte colony-stimulating factor (G-CSF) with each cycle and the lack of safety data on G-CSF in pregnancy. Tamoxifen and trastuzumab are contraindicated in pregnancy because of the high frequency of congenital abnormalities and poor fetal outcomes.

Radiation therapy may be a necessary treatment for some cancers during the prenatal period, but it is not recommended for patients with breast cancer until the postpartum setting. The effects of radiation on the fetus are dependent on both gestational age and fetal dose. The recommended fetal radiation dose is less than 0.05 Gy to avoid increased risk of malformations or lifetime cancer. The dose typically recommended for the treatment of breast cancer would exceed the fetal radiation dose in most cases and should be withheld until postdelivery. Radiation can safely be delayed until postpartum, with surgery and chemotherapy the first-line therapeutic options in the prenatal period.

Historically, modified radical mastectomy has been the surgical procedure performed in women diagnosed with breast cancer during pregnancy because of the concern about delaying radiation therapy until the postpartum setting. Several reports have been published showing that breast-conserving surgery with postpartum radiation can be performed with good outcomes (i.e., no apparent evidence of local recurrence at follow-up). Breast-conserving surgery may be delayed until the postpartum setting, with neoadjuvant chemotherapy given during the pregnancy, depending on the gestational age at presentation, clinical situation, and tumor stage.
Conclusions

The patient in this case presentation received doxorubicin and cyclophosphamide every 3 weeks for 4 cycles during the second and third trimester of pregnancy, with the last cycle given at 32 weeks’ gestational age. Her only complication during pregnancy was presumptive cholestasis of pregnancy with pruritus. She had an induced delivery at 37 weeks’ gestational age because of the fetus falling off the expected growth curve. The baby was born without any complications and is healthy. The patient had genetic testing and is BRCA1-positive. She is scheduled to receive paclitaxel therapy every 2 weeks for 4 doses in the postpartum setting, and will have surgery after completion of chemotherapy. She is currently expected to have a right modified radical mastectomy and a left total prophylactic mastectomy; however, she is waiting to make her final decision on the surgical plan until her follow-up imaging is performed after completion of the first cycle of paclitaxel.

Although breast cancer is rarely diagnosed during pregnancy, it is the most common malignancy associated with pregnancy. Clinicians must be aware of the multiple management and treatment options available and be able to counsel their patients on the risks and benefits to both patient and fetus. A team approach must be taken in developing the treatment plan, involving a medical oncologist, obstetrician, perinatologist, surgical oncologist, and radiation oncologist. The gestational age of the fetus at the time of diagnosis will also significantly influence the treatment plan. Further investigation is needed to clarify the safety of other anticancer therapies in pregnancy.

References