

Palpable right breast mass in a pregnant woman

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SUMMARY

Background A 29-year-old female presented with a palpable right breast mass at a 12-week prenatal visit. She had no family history of breast or ovarian cancer. Ultrasound revealed a 3 cm lobulated mass, which was confirmed to be malignant by a core biopsy. Postmastectomy pathology at 15 weeks' gestation demonstrated this mass to be a stage T2N0M0 high-grade invasive ductal carcinoma with 0/20 axillary nodes involved. A staging CT scan postpartum showed an enlarged right internal mammary lymph node, confirmed by MRI as suspicious for malignancy.

Investigations Physical examination, breast ultrasound, core biopsy, mastectomy, CT scan, MRI.

Diagnosis Pregnancy-associated breast carcinoma.

Management Mastectomy, chemotherapy and radiotherapy.

KEYWORDS breast cancer, chemotherapy, mastectomy, pregnancy, radiotherapy

CME

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THE CASE

A 29-year-old woman with a history of infertility who required intrauterine insemination was found to have a palpable right upper-inner quadrant breast mass during a routine 12-week prenatal visit. The mass had become noticeable and grown rapidly over several weeks prior to the prenatal visit. She had no pain, nipple discharge, fever, weight loss, or other symptoms. Physical examination 6 months earlier was normal and she had no family history of breast or ovarian cancer. Physical examination revealed a 4 cm firm, mobile right breast mass at the 2 o'clock position without skin dimpling, edema or nipple inversion, and with no axillary or supraclavicular lymphadenopathy. A mammogram was not performed on this patient because of pregnancy. Ultrasound limited to the right breast revealed a 3 cm lobulated hypoechoic mass at the 2 o'clock position, and malignancy was confirmed by a core biopsy. At 15 weeks' gestation, the patient underwent a right modified radical mastectomy at a large teaching hospital in the northeastern US. Pathology revealed a 3.5 cm invasive ductal carcinoma, grade 3 with negative surgical margins and negative axillary lymph-node involvement (0/20). The tumor was estrogen-receptor (ER) negative, progesterone-receptor negative, HER2/c-erbB-2 negative, and was pathologic stage IIA (T2N0M0).¹

Postoperatively, the patient elected to delay chemotherapy until after Caesarean section at 37 weeks' gestation. Postpartum contrast-enhanced helical chest CT identified an abnormally enlarged internal mammary lymph node (IMLN) (Figure 1). Bilateral breast MRI with ULTRASMAALL SUPERPARAMAGNETIC IRON OXIDE (USPIO) revealed an abnormally enlarged (1.8 × 1.1 cm) IMLN and a 0.5 cm hyperintense chest wall lesion, both suspicious for malignancy (Figure 2). The hyperintense findings on

post-USPIO imaging suggested malignancy, as macrophage internalization of iron oxide nanoparticles in benign nodes usually result in a lower mean signal intensity on fast spin-echo T2-weighted images. No systemic metastases were noted on either CT or MRI.

After dose-dense ACT chemotherapy comprising four cycles of concurrent doxorubicin and cyclophosphamide followed by four cycles of paclitaxel every 2 weeks with filgrastim, postchemotherapy MRI showed shrinkage of the chest wall lesion and IMLN. The patient then received radiotherapy to the right chest wall, IPSILATERAL SUPRACLAVICULAR FOSSA and IMLNs.

DISCUSSION OF DIAGNOSIS

Initial diagnosis

In any woman, the presence of a new dominant breast mass requires thorough evaluation. A medical history should include menstrual history, hormonal therapies (including oral contraceptives or fertility drugs), prior pregnancies, previous breast biopsies and family history of breast or ovarian cancer. In this case, it was known that the patient had not undergone any previous breast biopsies and her gynecological history was not thought to influence management, so was not elicited. Physical examination should include an evaluation of regional lymph nodes, a bilateral breast examination and an evaluation of the lungs and abdomen. Ultrasound can help determine whether the mass is cystic or solid.

In this case, the patient's history, physical examination at presentation, ultrasound findings and the reported rapid growth of the mass all indicated an invasive breast carcinoma. During pregnancy, breast cancer diagnosis and staging can be difficult because of changes in the breast tissue and concern for fetal safety. Ionizing radiation can potentially have teratogenic or carcinogenic effects, although with proper abdominal shielding, diagnostic chest imaging with mammography can be safely performed. The estimated fetal exposure to ionizing radiation with chest X-ray and mammography are <0.005 cGy and 0.007 – 0.02 cGy, respectively, with <0.5 cGy considered safe for the fetus. CT is not recommended during pregnancy, however, due to concerns that the increased dose of ionizing radiation could result in a minimal increased risk of childhood malignancy or abnormalities

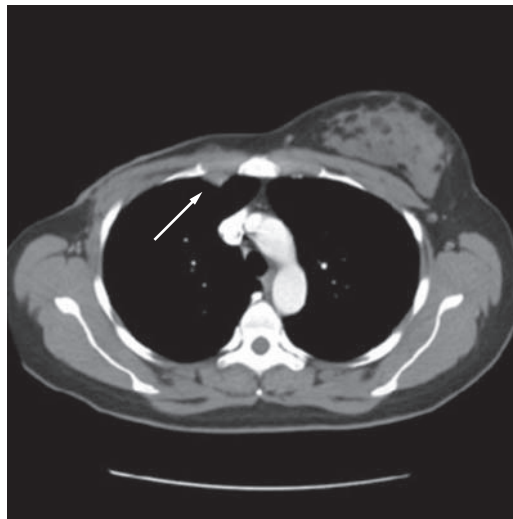


Figure 1 Postpartum contrast-enhanced helical chest CT scan showing an enlarged internal mammary lymph node (white arrow).

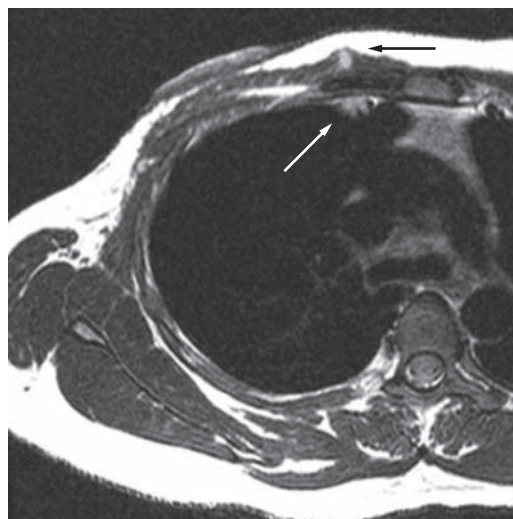


Figure 2 Breast MRI with ultrasmall superparamagnetic iron oxide demonstrates both the enlarged right internal mammary node (white arrow) and right chest wall lesion (black arrow) with hyperintensity, indicating a tumor.

in the developing fetus.² Mammography is helpful in identifying suspicious lesions in both breasts, but in this case the patient opted for mastectomy once core biopsy had confirmed malignancy, rather than receive any exposure to ionizing radiation.

Differential diagnosis

The main differential diagnoses of a breast mass during pregnancy include sarcoidosis, infection,

GLOSSARY

ULTRASMALL SUPERPARAMAGNETIC IRON OXIDE (USPIO)

MRI contrast used to detect functional, rather than architectural, changes to identify nodal metastases from solid tumors

ACT

Doxorubicin, cyclophosphamide and paclitaxel

IPSILATERAL SUPRACLAVICULAR FOSSA

Regional lymph nodes on the same side of the body as the tumor that are a potential site of nodal drainage from the internal mammary or axillary lymph nodes

GLOSSARY**AJCC STAGING SYSTEM**

A clinical and pathological staging system established by the American Joint Committee on Cancer to reflect prognostic factors for survival in most solid tumors, including breast cancer

SENTINEL LYMPH-NODE MAPPING

Minimally invasive surgery to assess lymph nodes most likely to be affected by the spread of a primary solid tumor

trauma and neoplasia. Most palpable breast masses in young women are benign neoplasms. Fibroadenoma is the most likely benign tumor in younger women, with papillomas or other benign tumors less likely. The rapid presentation of this patient's breast mass, however, made a malignant neoplasm more likely. A primary breast cancer was more likely than a metastasis, which tends to present with pain and multiple lesions in the breast or other parenchymal sites, most commonly the lungs and liver. In this case, core biopsy confirmed the diagnosis as a primary breast cancer.

TREATMENT AND MANAGEMENT**Staging and initial treatment**

Breast cancer diagnosed in the first trimester of pregnancy poses significant challenges and requires a coordinated, multidisciplinary approach. Despite concern regarding ionizing radiation during pregnancy, mammography can be performed with minimal fetal risk. Imaging the breast and regional lymph nodes with MRI eliminates the risks associated with ionizing radiation, but does expose the fetus to acoustic noise and may induce radiofrequency thermal heating.³ Gadolinium-enhanced breast MRI is increasingly used for staging and treatment decisions in breast cancer,⁴ but gadolinium is contraindicated during pregnancy because it crosses the placenta. MRI with USPIO has previously demonstrated accuracy in identifying clinically occult nodal metastases in other cancers⁵ and is under investigation in breast cancer, although it has not been tested during pregnancy. Imaging of the parasternal region with CT or MRI is not currently a routine procedure in patients with node-negative breast cancer, but may become increasingly important for full staging as the most recent AJCC STAGING SYSTEM requires evaluation of the IMLNs. Breast ultrasound may also be used for staging. SENTINEL LYMPH-NODE MAPPING is contraindicated in pregnancy because of the lack of safety data for Lymphazurin dye and possible aberrant lymphatic drainage in the pregnant breast. Chest radiography or CT can be helpful for staging metastases, and ultrasound is preferable to abdominopelvic CT for evaluating the liver if indicated. Imaging studies within 4 months of surgery are considered complementary to pathologic staging.¹ In this patient, it is unclear whether the regional IMLNs were involved initially or as the result of progressive disease.

Initial surgical options include mastectomy or lumpectomy. In this case, neoadjuvant chemotherapy in the early second trimester could be considered, in order to make lumpectomy easier to perform. If pregnancy is maintained, then lumpectomy risks higher local recurrence rates compared with mastectomy, because adjuvant radiotherapy is contraindicated during pregnancy. A presumed T2N0M0 breast cancer does not meet the usual criteria for postmastectomy radiotherapy (primary tumor ≥ 5 cm or ≥ 4 positive nodes) and thus would not be routinely recommended;⁶ however, according to the AJCC staging system involvement of the IMLNs upstages breast cancer to at least N2 disease.¹ In this case, postmastectomy locoregional and metastatic staging studies were deferred until the postpartum period to minimize any adverse effects on fetal health. Although CT or MRI findings indicating recurrence or more advanced disease usually warrant a biopsy to confirm the clinical staging, in this case, due to concerns regarding vascular or pleural injury, percutaneous biopsy was felt to be unsafe. The MRI findings in the chest wall and IMLN were reassessed after chemotherapy rather than surgically excising the node.

Adjuvant chemotherapy and radiotherapy

Based on the patient's age, tumor size, pregnancy and ER negative status at the time of diagnosis, it was recommended that she receive systemic chemotherapy. Although the patient's tumor appeared to be ER-negative, similar to the majority of breast cancers during pregnancy,⁷ the effects of estrogen might have more complex effects during pregnancy than in a non-pregnant patient. Doxorubicin and cyclophosphamide may be given safely during the second and third trimester, although there are potential risks to the fetus, including intrauterine growth retardation, transient leukopenia, malformation, or even fetal death.⁸ In this case, however, the patient declined to receive chemotherapy during her pregnancy and treatment was therefore scheduled to begin 2 weeks postpartum, after staging studies were complete. At the hospital where the patient was treated, the regimen of choice for chemotherapy off-protocol is dose-dense ACT and the patient was not a protocol candidate because randomized controlled trials generally require patients to begin cytotoxic chemotherapy within 3 weeks of surgery. In this case, because of her pregnancy, the patient did

not start chemotherapy until several months after surgery. In addition, despite complete surgical excision and negative axillary nodes, the patient had radiologic evidence of IMLN involvement, which increased the stage of malignancy from N0 to N2.¹ All these factors supported the use of adjuvant chemotherapy. A small randomized trial has suggested a trend toward increased distant recurrences after surgery if chemotherapy is delayed until after radiotherapy.⁹ The efficacy of delayed ACT chemotherapy with more advanced disease is, however, unknown.

Although isolated IMLN recurrences are rare after mastectomy and chemotherapy,¹⁰ two randomized trials demonstrated a survival benefit with the addition of postmastectomy radiotherapy of the IMLNs.^{11,12} Irradiation of the IMLNs can be technically challenging and is considered controversial because of the potential increased risk of cardiopulmonary injury. Whether including the IMLNs in postmastectomy radiotherapy fields improves its efficacy is currently under investigation in a randomized trial by the EORTC.¹³ In this case, because the patient had a negative axilla on axillary dissection, she received regional nodal irradiation to only the internal mammary chain and the medial supraclavicular fossa, which resulted in moderate fatigue and skin toxicity. Delayed adjuvant radiotherapy might be less effective in providing a survival benefit, but in a case such as this it may control the recurrence of the chest wall lesion and IMLN involvement. The patient underwent regular follow-up visits every 3 months with radiological and serological tests when required. Unfortunately, CT of the chest 6 months after radiotherapy demonstrated new pulmonary nodules and mediastinal adenopathy, with a biopsy confirming recurrent breast cancer.

CONCLUSION

Pregnancy-associated breast cancer is rare, but presents unique challenges in evaluation and management. An enlarging breast mass in a pregnant woman should be investigated with sonography and biopsy to establish a diagnosis. A multidisciplinary team can then proceed with staging and treatment after the patient has decided whether to terminate or maintain the pregnancy. This case highlights the challenges of balancing competing risks of fetal

and maternal health during pregnancy with the risk of recurrence caused by delaying adjuvant therapy. Mammography can be performed safely, but MRI may also be considered if the patient opts to avoid ionizing radiation. Mastectomy is the most effective local therapy in a patient too early in pregnancy to receive timely adjuvant radiotherapy. Staging studies might assist in deciding whether to continue with the pregnancy and proceed with adjuvant therapy. If pregnancy is maintained, adjuvant chemotherapy can be given relatively safely during the second and third trimesters. In more advanced breast cancers treated with mastectomy, postpartum radiotherapy may help to improve locoregional control and survival after mastectomy.

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GLOSSARY

EORTC

European Organization for Research and Treatment of Cancer

Competing interests

The authors declared they have no competing interests.