

Managing Breast Cancer Diagnosed in First Trimester Pregnancy: A Case Report

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Abstract

Introduction: Breast cancer is the most common malignancy in pregnant women, occurring at a rate of about 1 in 3000 pregnancies. Unfortunately, this will sometimes occur during the first-trimester of pregnancy and this situation warrants discussion of management options with regard to the mother and child, especially with the current trend of deferring child bearing to a later age. **Clinical Picture:** We present a 34-year-old primigravida who had a breast lump prior to confirmation of her pregnancy and received her diagnosis of invasive breast cancer at 7 weeks' amenorrhoea. The oncologic management options of this pregnant patient with breast cancer are discussed. **Treatment:** The patient eventually opted to undergo wide excision of the breast cancer with sentinel lymph node biopsy and possible axillary clearance together with termination of her pregnancy. **Results:** The patient successfully underwent surgery for her breast cancer and was subsequently treated with adjuvant therapy as per normal protocol for a non-pregnant patient. **Conclusion:** The management of breast cancer and pregnancy occurring concurrently is a complex problem fraught with many dilemmas for both the medical team, the patient and her family. The option chosen must involve a multidisciplinary team and have full informed consent of the patient.

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Introduction

Cancer complicates approximately 1 per 1000 pregnancies and accounts for one third of maternal deaths during gestation.^{1,2} The reproductive system is affected by malignant growth more frequently than any other systems during pregnancy. Pregnancy-associated breast cancer is defined as breast cancer diagnosed during pregnancy, lactation or 1-year postpartum. The median maternal age at the time of diagnosis of breast cancer during pregnancy is 32 to 38 years and the median gestational age at diagnosis is 17 to 25 weeks.² The management of a pregnant mother with cancer is difficult and complex with decisions to be made which can impact both mother and the unborn child. In addition, various ethical and religious issues complicate the final decision when the management of the pregnant patient with breast cancer is incompatible with continuation of gestation. Breast cancer is uncommon in young, premenopausal women especially as local data shows a peak increase in incidence during the fourth and fifth

decades of life in Singapore.³ However, the trend to defer childbearing to a later age will make the issue of pregnancy and breast cancer of increasing importance. This is because many more women will still be in the process of starting or completing their families when a discovery of breast cancer is made. We describe a case of breast cancer in a patient who was diagnosed during her first trimester of pregnancy (7 weeks amenorrhoea).

Case Report

Our patient was a 34-year-old Chinese woman, married for 7 years with no prior pregnancies, who presented with a painless, enlarging lump in the right breast to her doctor. On examination, a 2-cm discrete lump was felt in the upper outer quadrant of the breast. An initial ultrasonographic examination of the lump revealed benign features of a solid lump with macro-lobulation and no posterior acoustic shadowing (Figs. 1 and 2). She was subsequently referred to our centre for further management of her breast lump.

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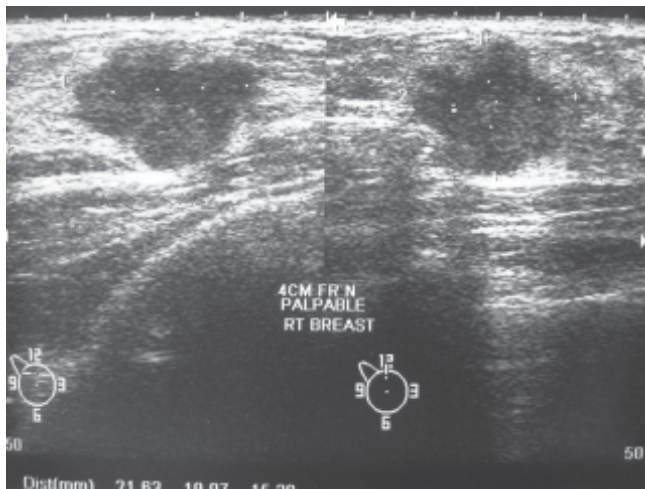


Fig. 1 Horizontal and transverse sections of the palpable lump at the 12 o'clock position on ultrasonogram. There is macro-lobulation, although there is no acoustic shadowing.

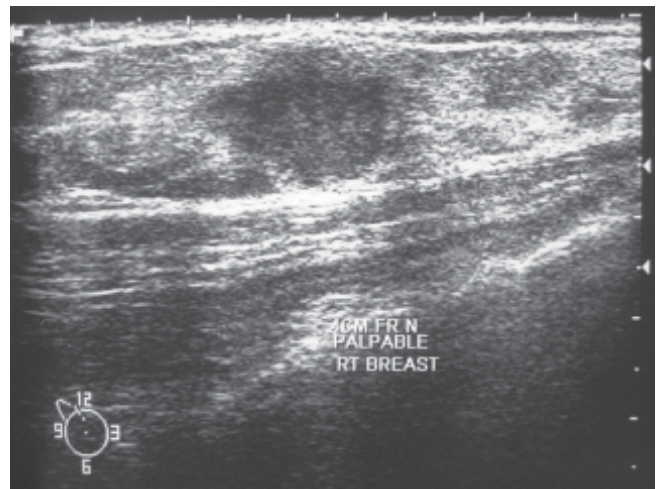


Fig. 2 Oblique section of the same solid lump on ultrasonogram. This view confirms features of uniform echogenicity and circumscribed margins.

Excision biopsy under local anaesthesia was scheduled and performed 2 weeks later. Prior to which she had suspected and confirmed her pregnancy. Clinically and radiologically the lump appeared benign, and as the patient was keen to have this lump removed entirely, she was scheduled for an excision biopsy and not a needle biopsy. Urgent histology requested due to suspicious intraoperative findings of a hard, gritty lump with an irregular appearance, revealed an invasive ductal carcinoma.

The patient was seen at 7 weeks' amenorrhoea to discuss management options of her breast cancer in pregnancy with a multidisciplinary team of surgical and medical oncologists, an obstetrician and breast care specialist nurse. Our patient was initially keen to manage her condition and continue with the pregnancy. Her major concerns and preferences included the following:

1. Wanting to keep the pregnancy, as it was a precious one.
2. Wanting the option of sentinel lymph node biopsy to assess the axillary nodal status, as she was worried about subsequent lymphoedema.
3. Wanting breast conservation surgery.
4. Not keen for any form of chemotherapy during pregnancy, as she was worried about its effects on the baby.

Various options and management plans were discussed with her. She was made aware that we would not be able to give radiotherapy during the pregnancy.¹ As for sentinel node biopsy, we were unsure about the effects of the radiation exposure to the unborn child and the use of blue dye is not approved for pregnant patients.^{1,4} The medical oncologists informed her that they were comfortable giving chemotherapy during the second and third trimester of pregnancy.⁵⁻⁸ She was also reassured that a general

anaesthesia for any surgical procedure was safe. She also sought a second opinion from a medical oncologist in another hospital. Her family especially her husband was also present at each clinic consultation and kept fully informed.

Eventually, she decided to terminate her pregnancy after detailed discussions. The patient requested for a lumpectomy with a sentinel lymph node biopsy (SLNB) for management of the axilla. Wide excision axillary clearance (WEAC) was finally performed instead as the first sentinel lymph node removed showed metastatic focus of tumour on frozen section intraoperatively. Suction termination of pregnancy was also performed in the same sitting.

Histology of the wide excision showed complete tumour removal with clear margins and confirmed a grade 3, invasive ductal carcinoma with positive oestrogen and progesterone receptor status. Only 1 axillary lymph node out of 18 removed contained metastatic disease. The products of conception confirmed fetal parts measuring 10 by 9 cm and a heel toe length of 0.6 cm.

Postoperatively, she was discharged well with no complications. She subsequently went on to undergo adjuvant chemotherapy, radiotherapy and hormonal therapy.

Discussion

Our patient's options were to continue with the pregnancy and undergo treatment tailored to balance maternal-fetal risks or to terminate the pregnancy and undergo conventional treatment.

The role of breast conservation surgery was discussed with this patient. It is generally not recommended, especially in a first trimester pregnancy, as it requires definitive postoperative adjuvant radiotherapy for adequate loco-

regional oncologic treatment.^{1,7} Although there are reports of similar survival rates with breast conserving surgery and mastectomy in pregnant women; none of the patients were diagnosed or had definitive surgery in the first trimester.⁸ Furthermore, delays in delivering adjuvant radiotherapy may impact on maternal outcome with higher local recurrence rates.^{1,7} Therefore, mastectomy remains the standard management of patients with early disease in first trimester pregnancies. A proportion of patients who undergo mastectomy, go on to receive radiotherapy as a consequence of large tumour size or multiply involved nodes. This occurs only after adjuvant chemotherapy is given and it is administered following delivery of the baby.^{1,7} Surgery and chemotherapy can be performed during pregnancy and for those with late second or third trimester pregnancies, radiotherapy could be given following delivery without too much delay.^{1,7} However, this was not the case for our patient.

Axillary clearance is preferred because nodal metastases are commonly found in pregnancy-associated breast cancers (due to the usually later presentation) and nodal status affects the need and choice of adjuvant chemotherapy. Our patient was keen to avoid morbidity from an axillary clearance and discussed SLNB as an option for management of the axilla. SLNB poses an unknown risk to the fetus as there is no current data on the effects of radiation exposure from the use of radiocolloid in pregnancy.^{1,7} The Panel of Consensus Conference on the role of SLNB in breast carcinoma advised against its use in pregnant women until more data was available.⁴ Isosulfan blue dye mapping is not recommended in pregnant patients because it has not been approved by the US Food and Drug Administration (FDA) and anaphylaxis has been observed with its use.^{1,4,7} Therefore in this patient, it would have been difficult to proceed with SLNB should she carry on with her pregnancy.

Our patient's excision biopsy had revealed a high-grade ductal carcinoma of at least 2 cm in size. She would therefore require some form of chemotherapy either neoadjuvant given before surgery or adjuvant after surgery. Chemotherapy has been shown to be safe when given during pregnancy especially in the second and third trimester after organogenesis.^{1,2,5-7} Major congenital malformations have been reported in the region of 2% to 3%.⁷ Most chemotherapeutic agents such as cyclophosphamide, anthracyclines and 5 fluorouracil used for the treatment of breast cancer are safe to be used during pregnancy. Methotrexate, however, has been reported to be an abortifacient especially when given during the first trimester. There has been limited experience with newer agents such as the taxanes except for case reports, and as such it is not currently recommended for use.^{1,2,7}

There are some series published which confirm the safety

in terms of peripartum complications and immediate fetal outcome with the use of chemotherapy for breast cancer.⁵ In addition evidence from the treatment of pregnant patients with leukaemia, administration of chemotherapy has not been shown to be deleterious to the child's development, with follow-up ranging to 17 years.^{9,10}

The use of hormonal therapy is usually reserved for after delivery in patients with hormone receptor positive cancers. There is no data on the use of either tamoxifen or an aromatase inhibitor in pregnant patients. Its use is therefore not recommended.^{1,2,7}

Indications for termination of pregnancy are both medical and social. The social indications can be affected by cultural, family and marital considerations. Underlying considerations include the demise of the mother while the infant is still young, the presence of a suitable main caregiver and family support. A pregnant woman with advanced disease and dismal prognosis may choose to have an abortion. Traditionally, pregnancy-associated breast cancer has been thought to have a poorer prognosis and proceeding with the pregnancy was believed to further aggravate the situation. This has let many to advocate termination of the pregnancy and then proceed with conventional treatment of the disease.^{1,7}

Although pregnancy-associated breast cancer has long been regarded as having poor prognosis, a recent study showed that the overall survival rate of patients with stage II and III disease was 75% (at a median of 40 months). This suggests that with modern multimodality therapy, outcome may not be as poor as was previously thought.² The previously observed poor prognosis could be explained by delayed diagnosis and presentation as pregnant patients tend to have a more advanced stage of disease than non-pregnant women. Most studies suggest little difference in survival between pregnancy-associated and non-pregnancy associated breast cancer when compared stage for stage.^{1,2,7} In historical series, no significant reduction in relapse rate or improvement in survival has been seen with termination of pregnancy. But it is possible that any potential benefit from termination was masked as women with poorer prognoses tend to opt for this.

There is definitely a role to manage breast cancer in the first trimester without termination of pregnancy. Thorough discussions with patient and family should precede any recommendations for therapy and result in understanding of the clinical circumstances, prognosis and therapeutic options available. Decisions must be made jointly, with the pregnant patient playing a central role. The presence of a skilled multidisciplinary oncologic and obstetric team, pivotal in the management of her breast cancer and pregnancy, is imperative. Ultimately, the decision on the management of the breast cancer and pregnancy should be

left to the patient, as all options have been explained, and various risks and complications fully understood. In this instance, the patient had planned this pregnancy. The patient has to come to terms with the diagnosis of breast cancer and also with the termination of her pregnancy. Throughout the process, psychological support for the patient and her family was necessary.

REFERENCES

1. Keleher AJ, Theriault RL, Gwyn KM, Hunt KK, Stelling CB, Singletary SE, et al. Multidisciplinary management of breast cancer concurrent with pregnancy. *J Am Coll Surg* 2001;194:54-64.
2. Berry DL, Theriault RL, Holmes FA, Parisi VM, Booser DJ, Singletary SE, et al. Management of breast cancer during pregnancy using a standardized protocol. *J Clin Oncol* 1999;17:855-61.
3. Seow A, Koh WP, Chia KS, Shi LM, Lee HP, Shanmugaratnam K. Trends in Cancer Incidence in Singapore 1968-2002. Singapore: Singapore Cancer Registry, 2004. Report no. 6.
4. Schwartz GF, Giuliano AE, Veronesi U. Consensus conference committee. Proceedings of the consensus conference on the role of sentinel lymph node biopsy in carcinoma of the breast, April 19-22, 2001, Philadelphia, Pennsylvania. *Cancer* 2002;94:2542-51.
5. Ring AE, Smith IE, Jones A, Shannon C, Galani E, Ellis PA. Chemotherapy for breast cancer during pregnancy: an 18-year experience from five London teaching hospitals. *J Clin Oncol* 2005;23:4192-7.
6. Giacalone PL, Laffargue F, Benos P. Chemotherapy for breast carcinoma during pregnancy: A French national survey. *Cancer* 1999;86:2266-72.
7. Loibl S, von Minckwitz G, Gwyn K, Ellis P, Blohmer JU, Schlegelberger B, et al. Breast carcinoma during pregnancy: international recommendations from an expert meeting. *Cancer* 2005;106:237-46.
8. Kuerer H, Gwyn K, Ames F, Theriault RL. Conservative surgery and chemotherapy for breast carcinoma during pregnancy. *Surgery* 2002;131:108-10.
9. Aviles A, Neri N. Hematological malignancies and pregnancy: a final report of 84 children who received chemotherapy in utero. *Clin Lymphoma* 2001;2:173-7.
10. Reynoso EE, Shepherd FA, Messner HA, Farquharson HA, Garvey MB, Baker MA. Acute leukemia during pregnancy: the Toronto leukemia study group experience with long-term follow-up of children exposed in utero to chemotherapeutic agents. *J Clin Oncol* 1987;5:1098-106.