

Breast Cancer In Pregnancy: Management Approach

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ABSTRACT

About 1-2% of breast cancers occur during pregnancy and lactation, and 7% of fertile women have one or more pregnancies after mastectomy for breast cancers. The high physiological activity of the breast in pregnancy causes the breast to be engorged. There is increased vascularity and lymphatic drainage from the pregnant breast assisting the spread of metastatic process to the regional lymph nodes. The clinical features of cancers of the breast in pregnancy are the same as in the non-pregnant patient. Pregnant patients tend to have a higher incidence of positive lymph nodes, however. Early diagnoses is made possible with awareness of this condition during pregnancy, routine self examination, adequate history, meticulous examination with liberal use of fine needle aspiration biopsy and when necessary open biopsy under local anaesthesia. As in non-pregnant patients all modalities of treatments are intelligently employed in the treatment of breast cancer in pregnancy. Radical mastectomy is well tolerated during pregnancy, and the results of treatment during pregnancy are the same, stage for stage as in the non-pregnant woman. The reported overall survival rate for breast cancer in pregnancy is poor, reflecting the more advanced stage of the disease at diagnosis. An approach to the management of breast cancer in pregnancy is presented by a case illustration and a review of literature.

KEY WORDS: Breast Cancer, Pregnancy, Management

Introduction

About 1-2% of breast cancers occur during pregnancy and lactation. Seven percent of fertile women have one or more pregnancies after mastectomy for

breast cancers and 70% of these subsequent pregnancies can be expected within the first five years.¹⁻⁷ Diagnosis is often delayed because of physiological changes masking the true nature of the lesion. This results in a

tendency for both patient and physician to misinterpret the findings and to procrastinate in deciding on biopsy.^{8, 9} The reported overall survival rate for breast cancer in pregnancy is poor, reflecting the more advanced stage of disease at diagnosis.^{7, 8, 10-16}

Breast cancer is the commonest cancer that occurs with pregnancy and lactation. Twelve percent of patients seen in an Ibadan series were either pregnant or lactating.¹⁷ As this cancer is relatively common in pregnancy, physicians need to be conversant with the treatment of this condition that puts two lives at risks of treatment. What is the best management approach to breast cancers in pregnancy? What should physicians advise the patient who has had mastectomy for breast cancer regarding future pregnancies? Should pregnancy be avoided, should it be terminated if it occurs? This paper reviews the principles of management of cancers of the breast in pregnancy.

Case Illustration

A 35-year-old woman presented with one-month history of a left breast lump. The lump appeared at about the third month of the first pregnancy in a 9-year old marriage and was rapidly progressive and painless. There was no spontaneous nipple discharge and no history of trauma. There was no history of breast cancer in the family. She had never used hormonal contraceptives.

Physical examination showed a well-preserved woman, no pallor and afebrile. Chest examination was normal. The left breast was significantly larger than the right and had a mass measuring 8cm x 5cm located in the

upper outer quadrant. The mass was firm, mobile and non-tender. No expression nipple discharge. There were enlarged matted non-tender apical group of axillary lymph nodes. The supraclavicular lymph nodes were not palpably enlarged and there was no oedema of the arm. Abdominal examination revealed an 18-week gestation and normal foetal heart sounds. The liver and spleen were not enlarged. No palpable supraclavicular lymph node enlargement. No arm lymph oedema. Haemogram was 14g/dl. Urea, electrolyte and liver function tests were within physiological ranges. Chest radiograph was normal. Abdominopelvic pelvic ultrasonography defined a viable fetus of 18 weeks of gestational age. The liver and other intraperitoneal organs were normal. Fine needle aspiration cytology showed malignant cells. Skeletal survey was not done. A diagnosis of advanced left breast cancer (Manchester stage 3) in the second trimester of pregnancy was made. An informed consent was obtained and she had Patey's modified radical mastectomy at the 20 weeks gestation. No form of adjuvant therapy was added. Histology of the mastectomy specimen showed a well-differentiated invasive intraductal carcinoma. The Patient was followed up clinically and with serial urea, electrolyte, liver function tests, haemogram and ultrasound. She delivered a live female baby weighing 2.8 kilogram's at 36 weeks gestation by spontaneous vaginal route. Chemotherapy was started immediately after delivery and the baby was put on artificial milk. The patient has remained well at one year of follow up.

Discussion

Breast cancer in pregnancy is not a common problem because breast cancer is uncommon in women younger than 15 years of age.^{1-5, 8, 16-19} Of all patients with breast cancers, only 1% - 2% are pregnant at the time of diagnosis.^{1-3, 18, 21-23} This figure is relatively higher in Nigeria¹⁷ (12%). This may be accounted for by the recent tendencies to defer childbearing until later in life with more gravid women attaining age-ranges during which breast cancer is common. The high physiological activity of the breast causes the breast to be engorged, obscuring early detection of breast lumps.^{3, 5, 7-9} The increased vascularity and lymphatic drainage from the pregnant breast assists the metastatic process to regional lymph nodes. These tend to aid rapid growing of breast cancers. At the time of diagnosis, therefore, about 60% - 70% of cases have already developed palpable lymph nodes in the axilla.¹⁻⁵ The majority of breast cancers in pregnancy, therefore present to the physician at a late stage. The advanced stage of the presentation of the disease in the pregnant patient has been attributed to multiple factors related to the above pathophysiological changes

The clinical features of cancers of the breast in pregnancy are the same as in the non-pregnant patient. Pregnant patients tend to have a higher incidence of positive regional lymph nodes. With positive nodes, the prognosis is poor and in all likelihood the neoplasm has metastasised at the time of the initiation of therapy.^{2, 5-7} Early diagnoses is made possible by increased awareness, routine self examination, adequate

history, meticulous examination with liberal use of fine needle aspiration biopsy and, when necessary open biopsy under local anaesthesia.

As in non-pregnant patients all modalities of treatments are intelligently employed in the treatments of breast cancer in pregnancy.⁴⁻⁷ Pregnancy and lactation are not contradictions to mastectomy. Treatment should be based on the stage of the disease as in the non-pregnant patient. Radical mastectomy is well tolerated during pregnancy, and the results of treatment during pregnancy are the same, stage for stage as they are in the non-pregnant woman. The timing of surgery for cancer of the breast diagnosed late in pregnancy is however, a source of debate. Generally the emphasis of treatment is for the welfare of the baby in the third trimester of pregnancy. A little wait to allow the foetus to mature or for preterm delivery has not been found to worsen the overall prognosis.² Some reports suggest that patients treated postpartum at this stage of pregnancy may survive longer than those treated in the second and third trimesters. This suggests that postponement of therapy for patients near term may be of benefit.^{18, 20} Some clinicians feel that localised breast cancer in the first trimester of pregnancy is a valid indication to recommend abortion. Therapeutic abortion has not been found to increase survival and the presence of a foetus does not compromise proper therapy in early stages. Similarly, therapy for localised disease in later pregnancy can be carried out when the diagnosis is made without pregnancy termination.^{3, 7, 10, 21} Some however believe that in adv-

anced breast cancer, therapeutic abortion is usually necessary to achieve effective palliation as surgical castration is believed to be the appropriate first step in the management of premenopausal women with disseminated disease. Castration would be useless, unless accompanied by therapeutic abortion to remove the placental source of hormones.^{4, 7} When pregnancy enters the third trimester the decision for pre-term delivery depends heavily on the patient's wishes and the urgency for palliation. A short wait until a viable foetus can be obtained might not be accompanied by significant progress of the neoplasm. Reports by Peters and Rosemond illustrate that termination of pregnancy has no effect on patients' survival.¹² In addition there have been no reports of metastases to the foetus as in patients with melanomas, lymphosarcoma and leukaemia.⁷ Ariel and others demonstrated that abortion does not improve survival rate in cancer of breast. Indeed patients who had abortions did worse than those who did not. Therapeutic abortion is not currently believed to be an essential component of effective treatment of early disease despite the theoretical advantage of removing the source of massive oestrogen production.^{5, 8, 12, 21}

Most cases of breast cancers in pregnancy present late. The usual treatment plan for these lesions coming for treatment at a late stage is administration of chemotherapy or radiotherapy followed in six weeks by mastectomy. All antineoplastic drugs are theoretically teratogenic and mitogenic. The use of cytotoxic drugs in pregnancy raises moral and philosophic questions. Their use can

result in abortion, foetal death, malformations and growth retardation.^{3, 7, 10} These possible dangers must be weighed against the possible detrimental effect to the mother of withholding treatment. There are usually three stages of embryogenesis. In the first two weeks the blastocysts are relatively resistant to teratogens. Large insults are required to kill the blastocyst. A surviving blastocyst will not manifest any organ changes. The second stage is stage of organogenesis starting from the third week of gestation to the eighth week. This is the most critical stage in which the foetus is highly susceptible to teratogens. The last stage is the stage of organ development and growth; the foetus and the different organs increase in size.^{6, 7} However, the brain and gonads continue to grow beyond the second stage. Exposure to teratogenic agents beyond the third stage can affect general foetal growth but will not produce organ specific morphological malformations. Drug responses vary among individuals because of differences in absorption, protein binding, excretion rate, as well as differences in placental transfer and foetal metabolism of the teratogens. Small intermittent doses of teratogens administered over a period of time may enable a system to safely metabolise the teratogens and prevent malformation. Unquestionably, the first trimester of pregnancy is when the foetus is most vulnerable to cancer chemotherapeutic agents.^{7, 10} Chemotherapeutic agents, especially the anti folates should not be given to the pregnant woman in the first trimester except if there is life-threatening disease that can be helped by the drug. For very advanced disease chemotherapy has been used after the

first trimester. Cancer chemotherapeutic agents should be considered teratogenic and should be avoided in the first trimester of pregnancy if at all possible.

Any radiation therapy to the abdomen should, as much as possible be postponed until after delivery. Evidence suggests that even an exposure of 3 to 5 cGy can result in an increase in benign or malignant tumours in the child after birth. Radiation doses in excess of 200cGy during the first twenty weeks of gestation will result in congenital malformations in the majority of foetus exposed.⁷ Some surgeon recommend artificial feeding of the infant ostensibly to avoid vascular enrichment in the opposite breast which may also contain a neoplasm.⁷

What should physicians advice the patient who has had mastectomy for breast cancer regarding future pregnancies? Should pregnancy be avoided or terminated if it occurs? The recommendations should be influenced by two key considerations. Whether pregnancy promotes recurrence of cancer and the opportunity of having been cured. Most metastases appear within a 3-year period before incurring pregnancy. Older literatures favoured abortion for a patient who conceived post mastectomy for cancer. Some recommended abortion as soon as a patient who had treatment for breast cancer becomes pregnant.^{11, 19} Recent reports however show that pregnancy need not be avoided or terminated among those patients who are apparently free of recurrence or residual cancer after undergoing treatment for carcinoma of the breast. No detrimental effect of subsequent pregnancy could be demonstrated even

among patients with positive axillary nodes.²¹ Some recorded improved prognosis for patients who become pregnant after treatment for breast cancer. The decision to become pregnant and the medical management of the pregnancy are best determined however by the stage of the cancer and how the malignant potential affects the prognosis. Careful consultation should be sought with all support personnel, which should include the husband, spiritual leaders, psychologist and all other necessary personnel who are important for the sake of the patient's survival and support of the child.

The prognosis depends on the stage of the cancer, histological type, the age of pregnancy and the type of treatment given. The best prognosis is with those early cancers in the first half of pregnancy.^{1-5, 7, 8-11} Survival is lower for cases diagnosed late in pregnancy compared to those diagnosed in the first trimester. Prognosis seems to be determined further by the nodal status and stage at the time of diagnosis. It is said that if the lesion is detected early, present less than three months, smaller lesion than 2cm, histology is non-anaplastic and no positive nodes; the chance of survival in this cases for the pregnant or non-pregnant patient is the same. If on the other hand there is involvement of the subareolar region, diffuse inflammatory carcinoma, oedema, or ulceration of the skin, fixation of the tumour to the breast wall, or involvement of the high axillary, supraclavicular, or internal mammary nodes, the prognosis is poor for both the pregnant and the non- pregnant^{1-3, 15,18-23}

We present this patient because of the rare nature of cancer of the breast

in pregnancy, the technicalities of the management and the possible results of the treatment. This patient was carrying a prized baby being the first pregnancy in 9 years after marriage in an elderly primip. Our old primip patient had stage 3 (Manchester staging) in the second trimester of a precious pregnancy. Her aspiration was for her doctors to do what they thought was suitable for her. In this circumstance we required sound judgement in the overall management. The main factors to be considered whilst treating a pregnant woman with breast cancer include: stage of the disease, histological type, number of living children, age of pregnancy, patient's wishes and physician judgement.

In summary breast cancer in pregnancy is relatively uncommon. Careful serial examination is still the cornerstone of detection and is even more important in pregnancy when the physiological alterations in breast tissue make evaluation difficult. A baseline breast examination at the time of the first obstetrical visit is critical. Evidences indicate that pregnancy does not augment the rate of growth or distant spreads of breast cancer and that abortion for women with breast cancer does not improve the prognosis. It has been established that once the diagnosis is made, stage for stage, the pregnant patient does as well as the non-pregnant patient. Prognosis is as good for females who become pregnant after mastectomy as for those who do not become pregnant. A multidisciplinary approach should be adopted in planning treatment. At all stages there should be a close collaboration among the patient, her husband and therapist. Options of

treatments should be explained in detail. Particular consideration must be given to the desire of the patient to have the child and to her religious values, especially when discussing termination of pregnancy.

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