



# Pregnancy-Associated Breast Cancer

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## 1. Purpose of Meeting

Although rare, pregnancy-associated breast cancer is the most frequent solid tumor during pregnancy. Physiologic breast enlargement during pregnancy as an initial sign of pregnancy and very low incidence of breast cancer in young pregnant women, together lead to delay in diagnosis.

The incidence is 1 in each 1000-3000 pregnancies. It means that the exposure of gynecologists to this form of breast cancer is very low either during residency or thereafter during their professional life. So it is essential to review all aspects of pregnancy-associated breast cancer with gynecologists so that they do not miss this rare but lethal curable cancer

## 2. Summary of Presented Findings

The majority of cases are very young, less than 40 years old, which means they are out of the screening age range. For older pregnant women, screening is not done both due to possible radiation exposure of fetus and low accuracy of mammography in pregnancy-induced highly dense breasts. Therefore, all the patients are symptomatic at presentation. Mass or ulcer in the breast, nipple or axilla; skin or nipple retraction, nipple scaling, unilateral uniduct spontaneous nipple discharge with any color, unilateral breast edema without or with redness (Peaud'orange) are the symptoms that bring the patient to her obstetrician. Thus, all pregnant women must be informed by their obstetricians about the possibility of breast cancer occurrence during pregnancy as well as all signs and symptoms of breast cancer. It should be noted that, stage by stage, the prognosis is the same as that of non-pregnant patients.

Among the three breast imaging modalities, sonography is the first imaging procedure used for symptomatic pregnant women. It can safely be done during all trimesters of pregnancy. As always, sonography can differentiate solid tumors from cysts. Simple cysts are always benign, although they may present as large masses. Since

there is no possibility for malignancy in these simple cysts, there would be no need for further follow-up because during the follow-up, their size and number can change or they may disappear spontaneously. These findings do not change our approach. In the case of large painful cysts, they can be aspirated using a needle either by surgeons or under the guide of sonography by a radiologist. On the other hand, if any solid mass is seen in the wall of a cyst, it is no longer a simple cyst and is considered as suspicious, thus classified as at least breast imaging reporting and data system (BIRADS) 4 needing immediate tissue diagnosis. Sonography, also, gives important information about solid tumors. By the evaluation of margins, vascularity, and elasticity, it can differentiate possibly benign tumor defined as BIRADS 3 from suspicious ones defined as BIRADS 4 or 5 that, again, need immediate tissue diagnosis. Well defined round or oval masses with fine margins without vascularity by Doppler evaluation and elastic, not rigid in elastography, are considered as possibly benign tumors or BIRADS 3 and can be followed by sonography instead of tissue diagnosis because the possibility of malignancy though not zero, is less than 2%. Sonography can, also, evaluate the lymph nodes in the breast and axilla; and diagnose the suspicious ones (thick cortex, round rather than kidney shape). If an LN is suspicious, tissue diagnosis is needed by needle biopsy which is usually done at the same time as the breast biopsy.

Despite its value for symptomatic patients (giving more information about symptomatic lesion), it should be noted that sonography is not at all a screening modality and must not be prescribed for non-symptomatic women of any age who consult obstetricians for checkup.

Screening mammography is not indicated during pregnancy. In the case of approved cancer or suspicious finding, that need tissue diagnosis, it can safely be carried out to evaluate the extent of cancer, multi-focality and concomitant contra lateral cancer; with the use of an abdominal shielding to protect the fetus. abdominal shielding to protect the fetus. Instead of 4 standard views, only a single

oblique view is taken to minimize the radiation dose which affects the fetus.

Breast MRI for breast tissue evaluation is always dynamic, with and without contrast. Because of the absence of radiation, simple MRI can be done in all trimesters of pregnancy. As there is a lack of information regarding safety of Gadolinium used as contrast in breast MRI, MRI with contrast is contra-indicated during pregnancy in the scientific text books. Meanwhile, expert consensus in 2009 found it safe and suggested the use of breast MRI when needed during pregnancy.

### 3. Diagnosis

Like non pregnant patients, trucut biopsy is the standard of care in pregnant women. Physiologic tissue changes induced by pregnancy may interfere with correct diagnosis. To lessen diagnostic error, in any request for pathology, it must be mentioned that the patient is pregnant.

### 4. Treatment

Treatment is not different from non-pregnant patients. Due to the presence of the fetus, some points must be respected to avoid fetal damage. Multidisciplinary team work is designed to provide the most likelihood of survival for the mother and her fetus, although as a rule, the mother's life always has priority over fetal life even if the fetus is a golden baby. Under no situation, treatment must be delayed to preserve the fetus. The only exception is the mother's request for the delay after full explanation to her about the danger of this delay for her own life.

### 5. Abortion

There is no place for abortion to improve the prognosis. In the first trimester, chemotherapy is contra-indicated because of its teratogenic effect during the organogenesis of fetus. So whenever chemotherapy is indicated during the first trimester, legal abortion must be done first to avoid fetal damage as the consequence.

Treatment may start with surgery, or chemotherapy is given at first as neo-adjuvant.

### 6. Surgery

Surgery can safely be done in all trimesters of pregnancy. The second trimester is the safest period for surgery since anesthesia may induce abortion in the first trimester

or premature labor in the third trimester. These simple facts dictate the need for the addition of a forensic medicine specialist and a perinatologist for repeated fetal evaluation and monitoring before and during the treatment. A neonatologist along with an equipped neonatal NICU must be available to increase the chance of neonatal viability in the case of premature labor.

Sever hyper emesis either post anesthesia or as a side effect of chemotherapy can also end the pregnancy either by abortion or premature labor.

Because of possible anesthesia induced fetal danger, surgery must not be done for diagnosis in pregnancy and like non pregnant women, needle biopsy is the standard technique for diagnosis. Even after confirmation of cancer by tru-cut biopsy, the patient and the family must be fully informed about the therapeutic plan and any potential side effects. Informed consents must be signed by the patient and biological father with the presence of a forensic medicine specialist.

A: Breast surgery: Breast surgery could be either conservative surgery or mastectomy. Due to presence of fetus, there is limitation for conservative surgery in early pregnancy.

B: Axillary surgery: Here It must be emphasized again that sentinel node biopsy is the standard of care for axillary staging in eligible cases with no clinical or radiologic suspicious lymph node.

It can safely be done even during pregnancy to avoid lymph edema as a side effect of axillary dissection. Despite injection of radioactive material (Technesium), for sentinel node detection, there is no danger of radiation exposure to the fetus. On the other hand, the use of blue dye is contra-indicated during pregnancy due to its possible anaphylactic shock as a side effect. Maternal shock of any cause, reduces fetal blood flow causing fetal damage or even death.

### 7. Radiotherapy

Two or three weeks must be passed conservative surgery can only be done: intra-epithelial cancers such as ductal carcinoma in situ, in which there is no need for chemotherapy, conservative surgery can only be done very late during pregnancy, 2 to 3 weeks before delivery. For other cases, there is no choice other than mastectomy For eligible cases with no clinical or radiologic suspicious LN, sentinel node biopsy can safely be done during pregnancy to avoid lymph edema which may occur as a result of axillary dissection

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use of blue dye is contra-indicated during pregnancy due to its possible anaphylactic shock possible shock as a side effect. Maternal shock of any cause, reduces fetal blood flow causing fetal damage or even death that reduces blood flow to fetus causing fetal damage.

## 8. Chemotherapy

Chemotherapy is absolutely contra-indicated during the first trimester due to its teratogenic effect at the time of the organogenesis of the fetus. If it is needed during the first trimester, legal abortion must be done prior to the administration of chemotherapy.

Chemotherapy has no proven danger for the fetus during the second and third trimesters. Attention must be paid to give chemotherapy 2 to 3 weeks prior to delivery so as not to have leukopenia or anemia and thrombocytopenia as a result of bone marrow suppression at the time of delivery.

Breast feeding is contra-indicated during chemotherapy.

## 9. Hormone Therapy

Any type of hormone therapy is contra-indicated during pregnancy.

## 10. Herceptin

Like hormone therapy, this type of targeted therapy is also contra-indicated during pregnancy.

## 11. Delivery

Breast cancer is not an indication for cesarean section. The type of delivery is chosen the same as in a normal pregnancy.

Chemotherapy can induce early menopause that, in some cases, can be permanent. Even if the menstruation returns it does not mean that the fertility has returned. For hormone positive patients, Tamoxifen must be given for 5 to 10 years which delays further pregnancy until completion of hormone therapy

## 12. Fertility Preservation for Newly Diagnosed Breast Cancer

Chemotherapy can induce early menopause that, in some cases, can be permanent. Even if the menstruation returns, for hormone positive patients, Tamoxifen must be

given for 5 to 10 years that can delay further pregnancy after the completion of treatment.

Fertility is considered as an important human right for all human beings including cancer patients. To respect this right, fertility preservation must be discussed for any young patient, especially young couples prior to the initiation of therapy right after the diagnosis has been made.

Young couples who are suitable for IVF have the best chance. Rapid induction of ovulation can be done safely in two weeks, right after diagnosis, followed by fetal banking. This fetus can be implanted in the uterus of the patient herself or someone else in the future.

Although donated sperm can be used for non-married women without any partner, it is not a routine task. For these patients desiring fertility preservation, either ovum or a wedge of ovary can be taken for future implantation, though the rate of future pregnancy is much less compared to IVF.

## 13. Pregnancy After Breast Cancer Treatment

In the majority of young patients, ovulation returns after the completion of treatment. There is no consensus for pregnancy after breast cancer treatment. Due to the mysterious role of estrogen in breast cancer, as a general rule, pregnancy was prohibited for breast cancer patients in any stage. Meanwhile there were patients that did not respect this recommendation. Strangely, prognosis of these patients was good with no increase in recurrence.

Nowadays, it is suggested that if the patient desires, she can become pregnant after 2 years following the completion of treatment. Even for hormone positive patients receiving Tamoxifen, it is permitted to discontinue Tamoxifen and become pregnant after 2 years of treatment.

## 14. Recommendation for Future Research

It should be noted that data on management and outcome of these patients in our country is very scarce and is a field in much need for research.

## 15. Names and Affiliations of Key Speakers

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- 2- Mehdi Jalali
- 3- Ramesh Omranipour
- 4- Masoumeh Giti