RESEARCH ARTICLE

BREAST CANCER AND PREGNANCY: HOW TO PROCEED?

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Abstract

Breast cancer is one of the most frequent solid tumors associated with pregnancy. The prevalence is constantly increasing with a high character and a greater frequency of advanced forms involving the maternal and fetal prognosis. Clinical, ultrasound, cytological and histological diagnosis of cancer, although slightly more difficult, is possible during pregnancy. The histological types encountered correspond to breast cancers encountered outside the pregnancy period. The prognosis of breast cancer does not appear to be affected by pregnancy, provided that it does not interfere with or delay the initiation of diagnostic and treatment procedures. Decisions should be made in a multidisciplinary meeting to ensure that the patient and her partner are as fully informed as possible about the consequences of the cancer and the possible impact of treatment on the future of their child. Breastfeeding should not be prohibited when the cancer is in complete remission. It is important to mention though that it is usually recommended that a woman who has breast cancer wait two years after completing treatment before allowing a subsequent pregnancy.

Introduction:

The association of breast cancer and pregnancy, i.e., breast cancer diagnosed during pregnancy and one year after delivery, is not rare. The incidence is estimated at 1/3000. If the frequency of late pregnancies over the next few years continues to increase, the number of cases of breast cancer in pregnancy will rise. The severity is related to the frequency of advanced inflammatory forms that threaten the maternal and fetal prognosis. It generates a conflict of interest between cancer and intrauterine life often psychological, social, ethical, religious and legal considerations as well as multidisciplinary medical decisions.

Histological aspects:

The proportion of so-called inflammatory forms and locally advanced forms is greater than in forms not associated with pregnancy. The histological varieties encountered in young women are the same whether or not they are pregnant.

The invasive ductal type is the most frequent (75-90% of cases), followed by the invasive lobular forms. The low expression of hormone receptors is specific to pregnant women: the proportion of non-hormone-dependent tumors is higher than in the absence of pregnancy.

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The progressive forms can be partly explained by the delay in diagnosis, which is more frequent in pregnant women and is estimated at 1 month compared to non-pregnant women, but also by the direct impact of steroids and various cytokines and growth factors on the neoplastic breast cells. The proportion of undifferentiated tumors during pregnancy is identical to that of non-pregnant forms for the majority of authors. The frequency of axillary histological invasion is differently assessed.

Clinical features:
Clinical diagnosis is difficult because of anatomical changes in the breast (hypervascularization, increased size, engorgement), more frequent mastopathies and a greater quantity of adenofibromas. Clinical examination of the breasts is therefore easier during the first trimester of pregnancy before breast engorgement related to hormonal impregnation. A more or less sensitive mass, skin involvement, and a mostly single ductal and bloody discharge should raise the diagnosis. Axillary adenopathy may be the cause of the diagnosis.

Paraclinical particularities and means of staging:
Mammography is discussed because it is criticized for irradiating the foetus and it seems however that the doses delivered to the uterus, provided a cover is used, are low. But it does not allow a correct diagnosis of malignant tumor during pregnancy because of gravid mammary imbibition. Ultrasound allows the recognition of a solid tumor, to appreciate its dimensions, as well as its single or multiple character. Ultrasound-guided biopsy allows to specify the nature of the tumor and to make the diagnosis with certainty. Finally, the assessment of extension during pregnancy is limited to a chest X-ray with abdominal protection and abdominopelvic ultrasound.

Treatment:
The medical-surgical treatment has two requirements:
- the treatment of the maternal disease without any prejudicial delay
- the respect of the embryo and the foetus at its various stages of maturation.

The chronology of the treatments must be adapted to the gestational age and the decisions concerning the different therapies must be taken only after multidisciplinary consultation and after having informed the couple. Surgery can be performed before the gestational age of 12 weeks. The classic treatment remains mastectomy with axillary curage. This surgical procedure is now considered as much as conservative treatment, either a clean lumpectomy performed in advanced forms, or an enlarged lumpectomy with axillary lymphadenectomy, on the double condition that radiotherapy is not delayed and that it is not toxic, taking into account the age of the pregnancy, the site of impact and the doses delivered.

However, the sentinel lymph node technique is prohibited because radioactive tracking is not permitted in pregnant women, but the alternative of a fluorescent method might be an option. Breast reconstruction cannot be considered during pregnancy due to physiological changes.

The teratogenic effect of anticancer agents is major in the first trimester, which makes chemotherapy contraindicated during this period. It is possible in the second and third trimester of pregnancy, taking into account maternal metabolic changes and transplacental passage of drugs. FEC, 5FU, adriyamicin and cyclophosphamide are the most commonly used protocols.

The last course of treatment should not be administered after 34 weeks of gestation, and there should be a three-week delay between the last course of treatment and delivery in order to avoid the birth of a neutropenic child.

Hormone therapy is contraindicated throughout pregnancy since treatment with antiestrogens would alter the hormonal environment of the fetus and result in teratogenic and lethal effects. Termination of pregnancy has no therapeutic effect on the mother and does not improve the probability of survival. Indeed, the influence of hyperestrogenism on maternal prognosis has not been proven, and hormonal receptors are often negative in pregnant women.

Obstetrical and postpartum management:
Before treatment is initiated, the gestational age and condition of the fetus will be assessed. Close monitoring of the fetus will allow rapid intervention in case of abnormality. Labor induction should not be systematic. Preferably, the delivery way will be vaginal, which presents less risk for the mother and less delay in the initiation of any
chemotherapy, unless there is an obstetrical indication for the c-section. No case of breast cancer metastasis to the fetus has been reported, but cases of placental metastasis have been observed.

Breastfeeding is prohibited during chemotherapy. If the patient wishes to breastfeed and if lactogenesis is maintained, a delay of at least four weeks after the last treatment is recommended before breastfeeding is resumed. The evaluation of fertility potential after chemotherapy is standard based on serum FSH/Inhibin B/estradiol/AMH levels and antral follicle count.

Finally it is important to mention that fertility preservation has undergone great progress, through in vitro fertilization and embryo freezing techniques, and must be discussed with every woman of childbearing age, diagnosed with breast cancer.

**Conclusion:**

The management of breast cancer during pregnancy must be decided on a case-by-case basis by a staff including surgeons, oncologists and neonatologists. The preventive approach of adapted contraception discussed with women diagnosed with breast cancer, remains the most effective way to avoid all kinds of complications.

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