FERTILITY AND BREAST CANCER

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1.INTRODUCTION

After breast cancer, about 70% of women of childbearing age want a baby, but treatments can be toxic to fertility; it is therefore estimated that only 10 to 15% of these women will develop a pregnancy after their breast cancer. [1,2]

2.BREAST CANCER AND HORMONES

Estrogens are a recognized growth factor in breast cancer, which is why hormonal disruption and high estrogen levels during pregnancy cause concern and even make pregnancy problematic. [3]

Since breast cancer is hormone-dependent, the occurrence of temporary or permanent amenorrhea after treatment is, for some, a therapeutic weapon and no longer just a toxic side effect. Prophylactic surgical or radiotherapy castration was widely used in the years 1960-1970. Is this amenorrhea of real therapeutic use? This question is still not resolved, however, radical and definitive hormonal deprivation is no longer appropriate. [4]

3.FERTILITY AFTER TREATMENT OF BREAST CANCER IN A YOUNG WOMAN

A woman's fertility can be impaired following the treatments implemented in the therapeutic strategy of breast cancer. [5,6]

4.SURGICAL TREATMENT

Breast cancer surgery, whether radical or conservative, has no impact on the patient's fertility. On the other hand, it is quite obvious that it has an impact on the woman's sexual life, especially in the case of a total mastectomy. [11]

5.CHEMOTHERAPY

The benefit of adjuvant chemotherapy is greater in women under the age of 50 than older. The indications are based on the European consensus of St. Gallen or the North American consensus of Bethesda: any patient under the age of 35 with an infiltrating breast tumor should benefit from adjuvant chemotherapy, whatever the other characteristics of their tumor. Chemotherapy frequently leads to amenorrhea and early menopause which will have an impact on the obstetrical future. [4,6, 9]

6.THE EFFECTS OF CYTOTOXIC AGENTS

There are acute and reversible toxic effects, in particular on the bone marrow, the appendages and the digestive tract. The medium or long term consequences, particularly on the gonads and reproductive function, are less well known.

Two common consequences of chemotherapy are amenorrhea and early menopause.

The toxicity of drugs can lead to a simple disturbance of hormone levels with conservation of menstrual cycles or to a definitive menopause.

At the tissue level, cytotoxic chemotherapy causes an absence of follicular maturation, ovarian fibrosis, or even follicular destruction.

The onset of amenorrhea is difficult to predict and will depend on the dose of cytotoxic agents administered and the age of the patient, the follicular capital inexorably decreasing during the woman's life, with a variable individual factor. [6-7]

7.FACTORS MODULATING THE INTENSITY OF THE EFFECT OF CHEMOTHERAPY ON THE OVARIES

- Drugs used: alkylating agents and cyclophosphamide are toxic to the gonads.
- Doses and duration of treatment: the reversibility of hypogonadism will depend on the cumulative dose of cytotoxic agents.

The role of the patient's age: amenorrhea rates are very different depending on the patient's age with a border between 35 and 40 years. Amenorrhea rates are low before age 35 and high after age 40. The older the age, the more a low dose is enough to induce amenorrhea. [7]

8. LOCOREGIONAL RADIOTHERAPY

Irradiation in the treatment of breast cancer may concern the treated breast, the wall or the axillary, supraclavicular and internal mammary lymph node areas. Diffused radiation to the pelvis is possible but negligible, which cannot cause ovarian failure. [7]

9.HORMONE THERAPY

9.1. TAMOXIFEN

Hormone therapy with tamoxifen (an antiestrogen with weak estrogenic activity) leads to irregularities in the menstrual cycle, which is generally respected, so fertility is retained as part of treatment with tamoxifen alone. Tamoxifen being teratogenic in animals, it requires effective contraception and because of its prescription period (5 years), therefore differs the possibility of pregnancy. [8]

9.2. THE OVARIOLYSE

Castration is most often temporary and reversible by analogues of LHRH; it is readily associated with tamoxifen in women under 35 (if positive hormone receptors). [9]

Influence of pregnancy after treatment for breast cancer on the prognosis of the disease and patient survival:

The literature highlights concordant studies which confirm that the prognosis of breast cancer is not altered by the occurrence of a subsequent pregnancy.

10. HOW LONG BEFORE A PREGNANCY AFTER BREAST CANCER?

The delay between the date of breast cancer and the first conception is on average around 2 years. The early pregnancy compared to the diagnosis does not influence the prognosis of cancer. [1,5, 10, 12]

The time period usually recommended to patients is based on the time of occurrence of regional recurrences and metastases. The median occurrence of local recurrences is 30 to 36 months and almost always in the first five years. As for metastases, 50 to 75% appear in the first two years and 65 to 85% in the first three years. It is for this reason that it seems reasonable to propose a period of 2 to 3 years before authorizing a pregnancy for women who have had breast cancer with a good prognosis (N-) and 5 years in the case of poor prognosis (N +). This wait-and-see policy prevents the concomitant occurrence of pregnancy and a recurrence or metastasis, the treatment of which is more uncertain during pregnancy.

The second argument is to prevent the unborn child from the risk of early death of his mother, in the event of a tumor with a good prognosis, pregnancy cannot be discouraged regardless of its time in relation to breast cancer; in the event of illness at risk of relapse, pregnancy does not modify this risk but a waiting period of 2 to 3 years seems reasonable.

Thus, the importance of the delay is more correlated with the prognosis of the disease itself than with a potential effect of pregnancy on the prognosis itself. [7.1]

11. INDICATIONS FOR THERAPEUTIC TERMINATION OF PREGNANCY

These numerous studies show that the termination of pregnancy, whether voluntary or not, does not influence the prognosis of breast cancer. When a pregnancy occurs after treatment for breast cancer, it must be accepted even if the period of caution has not been observed, since it does not influence the prognosis of the disease.

The indications for therapeutic termination of pregnancy are: unwanted pregnancy, breast cancer with a very poor prognosis or the need for radiotherapy or chemotherapy treatment of a local or distant course discovered during pregnancy. [14]

12.ASSESSMENT TO BE CARRIED OUT BEFORE PLANNING A PREGNANCY AFTER BREAST CANCER

When a pregnancy is planned, it is advisable to carry out before its initiation, a complete assessment of extension including a mammography, a hepatic and pelvic ultrasound, an X-ray of the thorax, a bone scintigraphy,

an assay of the tumor markers and possibly a brain scan. [14,15]

13.MONITORING OF PREGNANCY AFTER BREAST CANCER

Pregnancies occurring after breast cancer have no particularity when compared to pregnancies that occur in a matched population, not treated for breast cancer. There is no indication to perform a fetal karyotype, even if the patient has received chemotherapy. [7, 14]

14.BREAST FEEDING AFTER BREAST CANCER

Breastfeeding is possible in case of mastectomy, with the contralateral breast. [1,9] In the case of conservative surgical treatment, followed by external radiotherapy, the treated breast is generally no longer functional. In case of breast reconstruction with contralateral symmetrization surgery, breastfeeding is not contraindicated, but not recommended due to the risk of alteration of the aesthetic result. [13]

15.TERATOGENICITY OF TREATMENTS FOR CHILDREN

A prospective study did not show an increase in chromosomal abnormalities in children of mothers who had breast cancer treated with chemotherapy. It is not necessary to perform a fetal karyotype.
For tamoxifen, animal studies have shown damage to the genital tract in fetuses exposed in utero. Contraception is therefore essential in any premenopausal woman treated with tamoxifen. [2. 9,15]

16.CONCLUSIONS

Based on the available literature, no harmful effect of pregnancy after breast cancer has been demonstrated in terms of survival. All the published studies are consistent on the fact that the prognosis of breast cancer does not change when pregnancy occurs later. Termination of pregnancy after breast cancer does not affect the prognosis of the disease. Pregnancy should not be encouraged, contraindicated or terminated when it occurs in a patient previously treated for breast cancer and in complete remission. It seems reasonable to suggest a period of 2 to 3 years before authorizing a pregnancy for women who have had good prognosis (N-) breast cancer and 5 years in cases of poor prognosis (N +). This wait-and-see policy prevents the concomitant occurrence of pregnancy and a recurrence or metastasis, the treatment of which is more uncertain during pregnancy.
The second argument is to prevent the unborn child from the risk of premature death of his mother. Thus, the importance of the delay is more correlated with the prognosis of the disease itself than with an effect that pregnancy could have on the prognosis. Therapeutic abortions should only be offered in two situations: when the maternal prognosis is very unfavorable and in the event of progression of the disease if the necessary therapies are aggressive for the fetus.

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