

Pregnancy after Breast Cancer

Paula Cortiñas de Sánchez



“Ever since dawn was meant to be dawn, you are all
mother. Deeply wanted the moon full.
In your moon pain I have seen two women,
and a bare chasm in a serene light”.

Desde que el alba quiso, Miguel Hernández, 1939.

Breast cancer is the most frequent neoplasm in women, representing 25% of all neoplasms in this genre worldwide. Approximately 1.67 million new cases have been diagnosed for 2012 according to Globocan¹. Of all of them, about 20% are detected in women under 44 years of age, many of them still without descendants. In recent decades, the increase in the number of cases in younger women, combined with the delay in the age of the first birth, has made pregnancy after breast cancer an increasingly frequent topic in cancer treatment forums.

Preservation of fertility in these patients presents specific considerations. In case of cryopreservation of ovules or embryos, this is done by inducing ovulation with protocols that generate the lowest estrogen level during the stimulation, avoiding a progression of the disease before starting the cancer treatment. Likewise, gonadotrophin releasing hormone (GnRH) agonist analogs have been used in order to preserve ovarian function.

Fertility preservation in breast cancer patient is becoming more frequent, so it is of utmost importance to define the impact that pregnancy would have on survival and recurrence of the disease, in order to recommend the patient to seek descent with confidence. These considerations are of particular importance in breast cancer patients with positive estrogen and/or progesterone receptor (ER and PR +) and in patients undergoing adjuvant endocrine therapy.

In 2011, Hatem Azim et al.² conducted a meta-analysis on the safety of pregnancy after breast cancer and found that it was not related to a deleterious effect on the disease. On the other hand, a significant increase in overall survival compared to patients who did not become pregnant was observed. Just as breast cancer during pregnancy is considered to be of unfavorable prognosis, it would appear that the complex hormonal and immunological changes that occur during gestation have a positive effect on the patient with treated breast cancer. To explain this finding, the theory of alloimmunization has been proposed, since fetal and breast cancer cells share antigens, so that the mother's immune system would recognize them as strangers and prevent the growth of dormant tumor cells.

At the annual meeting of the *American Society of Clinical Oncology* (ASCO) in June 2017, a multicenter, retrospective, long-term follow-up study was conducted to evaluate the effect of postnatal pregnancy on breast cancer for an average follow-up of 12.5 years³. 1,207 patients, 333 pregnant and 874 patients who did not get pregnant were evaluated. When comparing both groups, there was no difference in disease-free survival in patients with ER+ (HR: 0.94, p = 0.68), ER- (HR: 0.75, p = 0.10), and in all patients (HR: 0.85, p = 0.15). There was also no difference in overall survival in ER+ patients (HR: 0.84, p = 0.32). However, there was a greater overall survival in pregnant women with ER- (HR: 0.57, p = 0.01) when compared to those who did not become pregnant after the disease, which resulted in an increase in overall survival of 28% when all patients were considered together (HR: 0.72, p <0.029). The authors conclude that pregnancy after breast cancer has no influence on the course of the disease and should not be contraindicated if the patient wishes, regardless of the state of the hormonal receptors.

It is important to take into account several considerations. To date, it has not been determined which is the safe interval of time after the end of the cancer treatment to plan a pregnancy. It seems that pregnancy in the short term is not safe, but in the long run is. In a subgroup analysis performed in the meta-analysis of Azim and col², pregnancy after 2 years did not have negative effects in terms of recurrence and overall survival, however, before the 2 years of treatment appears to have a deleterious effect. Probably the processes of angiogenesis and breast remodeling during pregnancy would have a negative impact on a breast that is not fully recovered.

It should also be noted what has been called the "Healthy mother effect", which considers that only women who are healthier and have a lower probability of relapse would be pregnant, so the best prognosis of those who have a gestation after cancer is due to a

more advantageous baseline health condition compared to those who fail to become pregnant and not to the effects of pregnancy. Either way, it would then seem advisable to wait at least two years after completing the treatment to achieve pregnancy and give it a chance to be consolidated, ruling out the risk of a relapse.

On the other hand, the treatment of breast cancer includes, in the case of patients with ER+ breast cancer, adjuvant endocrine therapy, which is a formal contraindication for pregnancy. This treatment requires at least 5 years, with an eventual extension up to 10 years, especially recommended in young women. In most patients, it is not an option to wait until endocrine adjuvant treatment is completed and then to become pregnant, as age increases the medical and obstetric complications of pregnancy. For this reason, the POSITIVE Study (Pregnancy Outcome and Safety of Interrupting Therapy for Women with Endocrine Responsive Breast Cancer) is being carried out, which will evaluate if the temporary interruption after two years of endocrine therapy during the period required by the patient to achieve pregnancy and breastfeeding, subsequently restarting adjuvant hormonal therapy, has some incidence on relapse and disease-free interval. In the case of patients with ER- breast cancer, since it does not require adjuvant endocrine therapy, the patient may become pregnant two years after completion of cancer treatment.

According to these studies, pregnancy is safe after completion of treatment for breast cancer and future gestation can be recommended in a patient successfully treated after two years. In the case of patients receiving tamoxifen, the current recommendation is to complete the five years of adjuvant endocrine therapy, pending on the results of the POSITIVE study. A pregnancy before that period is an exclusive decision of the patient and, in that case, endocrine therapy should be immediately restarted after the lactation period.

Nowadays, a gestation after breast cancer, in patients without active disease, is considered safe. The first patients who dared to have children after facing a breast cancer, avoiding the myth that rejected the safety of a pregnancy, each of them have allowed to count to form a valuable evidence that currently agrees to recommend, without fear, to complete the offspring in survivors of this neoplasm. Oncologic therapy has gradually been adapted to the needs of patients who have decided that life, after breast cancer, deserves to be fully enjoyed.

* Specialist in Gynecology. MgSc in Human Reproduction. Coordinator of the Cervical Cancer Prevention Program in Salud Chacao. Instituto de Oncología Luis Razetti and Clínica Santa Sofía, Caracas, Venezuela.

References:

1. Globocan, 2012 IARC. http://globocan.iarc.fr/old/age-specific_table_n.asp?selection=211862&selection=224900&title=Venezuela%2C+queWorld&sex=2&type=0&stat=1&window=1&sort=0&submit=%C2%A0Execute
2. Azim HA et al. Safety of pregnancy following breast cancer diagnosis: a metaanalysis of 14 studies. Eur J Cancer 2011;47:74

Intervalibre

3. Lambertini M et al. Safety of pregnancy in patients with history of estrogen receptor positive breast cancer: long-term follow-up analysis from a multicenter study. J Clin Oncol 35, 2017 (suppl; abstr LBA10066)http://abstracts.asco.org/199/AbstView_199_189078.html