

Ovarian Metastasis of Breast Cancer Found During Ovarian Tissue Cryopreservation for Fertility Preservation: A Case Report

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ABSTRACT

We present the case of a patient with ovarian metastasis of breast cancer revealed during ovarian tissue cryopreservation for fertility preservation in an University Hospital. The patient was a twenty-eight years old woman with a breast cancer had a laparoscopy for ovarian tissue cryopreservation. Ovaries revealed normal aspect on CT scan and during laparoscopy. Unexpectedly, pathological analysis of ovarian tissue revealed a breast cancer metastasis within the cortex, while the medulla was sane. This case report confirms the possible complexity of organizing optimal oncologic management and fertility preservation under time pressure.

Keywords: *Oncofertility, Ovarian Tissue Cryopreservation, Breast Cancer, Ovarian Metastasis, Fertility Preservation*

Introduction

Breast cancer is the most common female cancer even during the childbearing age (Ferlay *et al.*, 2015). Thanks to prevention, diagnosis and therapeutic advances, the mortality rate of breast malignancies keeps declining (DeSantis *et al.*, 2015). As a result, problematics related to survivors' quality of life have become a major concern (Letourneau *et al.*, 2012). In young patients, fertility issue is in the forefront (Bloom *et al.*, 2004). Evidence indicate that post cancer fertility is markedly decreased as a consequence of both the direct gonadal toxicity of chemotherapy regimens and the time needed before pregnancy (Bedoschi *et al.*, 2016). In this context, oncofertility counselling is now integral part of the management of young breast cancer patients (Hashimoto *et al.*, 2017). Recommendations state that this consultation should be organized as soon as possible following the diagnosis of malignancy (Oktay *et al.*,

2018). The timing before initiating cancer treatment leads to choose between oocyte or embryo vitrification after controlled ovarian stimulation, or ovarian tissue cryopreservation (OTC). Nowadays, in France, controlled ovarian hyperstimulation is often contraindicated for patients who require as soon as possible a neoadjuvant chemotherapy (Sallem *et al.*, 2018). OTC becomes more and more used, with at least 100 births already published.

We herein report the case of a young breast cancer patient in whom urgent OTC was performed, finally revealing the presence of unexpected ovarian metastasis.

Case Presentation

The case report is from the department of reproductive medicine, Hospital Jean Verdier, Bondy, France. Institutional review board approval was not required by the institution. The patient was a 28-year-old female who was diagnosed with grade 2 invasive ductal breast carcinoma. Her personal medical history included one abortion. She reported no family history of cancer. Estrogen or progesterone receptors, nor HER2 were highly expressed. The brain, thoracic abdominal and pelvic CT scans did not find any metastasis. The patient was then referred to an oncologic hospital. Physical examination revealed a lump of the whole right breast, with redness and extension to the chest wall. There were also right metastatic lymph nodes and 2 other suspect lumps in the left breast. Biopsies of both breasts confirmed the initial diagnosis. A whole-body PET scan was scheduled but was not available before 10 days.

According to the French recommendations, the patient was referred for oncofertility counselling before the initiation of cancer treatment (APHP, 2018). Markers of the follicular ovarian status measured on cycle day 12 revealed reduced ovarian reserve with serum AMH levels at 0.6 ng/mL and 7 small antral follicles counted on both ovaries. After counselling, due to the timing of chemotherapy and the neoadjuvant situation, ovarian tissue cryopreservation (OTC) was the chosen option. In our routine practice, we offer this technique in combination with oocyte vitrification after *in vitro* maturation (IVM). After informed consent, the patients opted for IVM combined with OTC and further administration of GnRH analogues during chemotherapy.

Laparoscopic right oophorectomy after transvaginal immature oocyte retrieval was then performed. The ovary looked macroscopically normal. No complication had been reported after the surgical procedure and 4 matures eggs as well as 22 strips of ovarian cortex were cryopreserved. Unexpectedly, pathological analysis of ovarian tissue revealed a breast cancer metastasis within the cortex, while the medulla was clear. The final stage of the cancer was T4cN2M1 based on the PET Scan. Despite chemotherapy, the patient did not respond to treatment and died 6 months later.

Discussion

Fertility preservation is nowadays an integral part of the initial management of young cancer patients. Among Fertility Preservation techniques available in pubertal women, oocyte vitrification following controlled ovarian hyperstimulation represents the most established and efficient method (Committee of American Society for Reproductive Medicine, 2013). However, OTC may also represent a more and more realistic option, even if the transplantation is still considered experimental (Donnez and Dolmans, 2017). The diagnosis of cancer often implies relatively urgent treatment. Therefore, fertility preservation represents a race against time. Whatever the technique chosen it is important to eliminate the presence of malignant cells within the ovary. In addition, when OTC is performed, the risk will be at the time transplantation with possible reintroduction of cancer cells and further recurrence of the primary disease. The main risk factors of ovarian metastases are a tumor >5 cm, inflammatory breast cancer, and the time frame between breast cancer diagnosis and oophorectomy (Peters *et al.*, 2017). Therefore, this patient should have been considered at risk for ovarian tissue grafting.

Apart from these oncologic risks, oncofertility also needs balancing the benefit and risks of FP techniques especially in case of life-threatening diseases and poor prognosis (Lambertini *et al.*, 2017; Partridge *et al.*, 2010).

The present case report points out many key questions in oncofertility. The time pressure for both oncologists and gynecologists led to organize the oncofertility counselling and urgent OTC before the final assessment of tumor extension. If the cancer stage was known before the oncofertility counselling, we could have avoided this surgery procedure.

Although the diagnosis of ovarian metastasis remains crucial, it may represent a difficult issue. Indeed, ovarian metastases are typically solitary and most often clinically asymptomatic (Peters *et al.*, 2017). These characteristics, and their disappearance with chemotherapy, may explain that the prevalence is probably underestimated. They appear most of the time years after the initial disease (Peters *et al.*, 2017; Bigorie *et al.*, 2010; Pimentel *et al.*, 2016). The prevalence of ovarian metastases of breast cancer is estimated between 13 and 47% on postmortem analysis (Bigorie *et al.*, 2010; Perrotin *et al.*, 2001; Bastings *et al.*, 2013). However, a recent study conducted in The Netherlands, found 2.4% of ovarian metastases in oophorectomies performed in breast cancer patients aged less than 41 years old. Thus, the risk of having malignant cells in ovarian tissue recovered for cryopreservation remains very low (Bastings *et al.*, 2013). A limitation for drawing such a conclusion could be the limited number of samples analyzed before cryopreservation. Data from patients having undergone ovarian tissue transplantation confirms the very low risk with only one local recurrence, probably independent from the graft

(Rosendahl *et al.*, 2011). With advances in *in vitro* follicular growth, the graft will not be mandatory anymore for restoring fertility. Therefore, tracking ovarian metastases will probably become more obsolete.

Conclusion

Fertility preservation represents an important issue for young women diagnosed with cancer. However, both oncologists and specialist in reproductive medicine are submitted to an extreme time pressure, which could sometimes lead to unexpected suboptimal management.

Conflict of Interest: None

Authorship: F.K. participated in the collection of data and contributed to writing the manuscript. C.S. was involved in the collection of data, the design of the study and contributed to revising the manuscript. M.G. participated in the design of the study, collection of data, and critical revision of the manuscript.

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