



## OVARIAN METASTATIC BREAST CANCER: ABOUT 3 CASES AND REVIEW OF THE LITERATURE

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### ABSTRACT

The frequency of ovarian metastases in breast cancer patients is varied according to the authors and type of series with figures ranging from 13.2 to 37.8%. The adnexal metastases of breast cancer often present a diagnostic and therapeutic difficulty. The complete surgical resection of these metastases seems to bring a benefit in terms of survival. This benefit is, moreover, a function of the residual tumor volume and the free interval between the initial diagnosis of breast cancer and the appearance of adnexal metastases.

**KEYWORDS:** Breast cancer, ovarian metastasis, treatment.

### INTRODUCTION

The ovaries are a frequent metastatic site of gynecological and extra-gynecological cancers, of which neoplasias of the digestive tract and mammary neoplasias are the main providers.<sup>[1]</sup> In addition, the discovery of an ovarian mass in a patient followed for breast cancer, asks the clinician the question of its primitive or secondary origin. We wanted to specify, in the light of the literature, the incidence of such an association, define the characteristics of metastatic cancers at the ovary and ask us about the need for a systematic search for these metastases during the assessment initial extension.

### PATIENTS AND METHODS

This is a retrospective study conducted over a period of one year, from July 1, 2017 to June 30, 2018 at the level of the gynecology department of the Mohamed VI center for screening and treatment of cancers, the IbnRochd University Hospital Center from Casablanca. Of 92 patients who had been operated on for ovarian tumor, the diagnosis of ovarian metastasis from breast cancer was retained in 3 patients, which makes us 3.2%.

### RESULTS

#### First observation

It is about Mrs. S.K, aged 44 years, followed for 6 months for a lobular invasive carcinoma multicenter of the right breast, for which the patient had benefited from a right Patey. As part of an extension assessment an endovaginal ultrasound was requested, and had shown minimal effusion with enlarged ovaries containing multiple cysts, the CA 125 blood test was normal. The

rest of the extension checkup showed no other anomaly. Laparoscopic exploration was proposed, with an intraoperative appearance of peritoneal carcinomatosis with tumor-like ovaries, several peritoneal implants, and minimal effusion. Ovarian and peritoneal biopsies were performed, with anatomopathological analysis in favor of a mammary lobular adenocarcinoma (strong expression of hormone receptors, diffuse labeling of CA15-3, massive expression of cytokeratin 7, and negative for the cytokeratin 20). Chemotherapy has been proposed based on FEC 100 (five fluorouracil, epirubicin 100mg / m<sup>2</sup>, cyclophosphamide) which is still in progress.

#### Second observation

It is about Mrs. G.B, 36 years old, single - patient eager for pregnancy -, having as antecedents a maternal cousin followed for breast cancer. The patient has been followed for 2 years for an infiltrative ductal carcinoma of the right breast whose immunohistochemical profile is luminal A, for which she had a right Patey, radiotherapy and tamoxifen hormone therapy. As part of a control assessment a pelvic ultrasound was requested, showing a heterogeneous right adnexal mass of fleshy consistency, the abdominopelvic scan showed a fleshy right paracerebral mass of 6cm long, with macro nodular contours. Surgical exploration by laparotomy has been proposed showing a solidocystic right ovarian tumor mass with minimal effusion. The blood test of CA125 was high at 250 IU / ml. A right adnexectomy, an omentectomy, and a peritoneal biopsy with contralateral ovary biopsy were performed, with the anatomopathological analysis of ovarian metastasis aspect of a mammary ductal adenocarcinoma, the remaining histological specimens were free from any

tumor proliferation. Chemotherapy has been proposed based on 5 fluorouracil + Doxorubicin + Cyclophosphamide.

### Third observation

It is about Mrs KH, 53 years old, menopausal, followed since 5 years for a lobular carcinoma infiltrating of the right breast of immunohistochemical profile type luminal B, treated by surgery (Patey right), radiotherapy, chemotherapy and hormonotherapy (with type of tamoxifen); whose initial expansion budget was without anomalies. The patient had consulted for abdominal distension, with an endovaginal echocardiographic mass a heterogeneous solidocystic pararenal mass, associated with a large effusion. The abdominal CT confirmed the presence of two 58-mm and 67-mm paraperitoneal fleshy masses respectively with macronodular contours. The blood test of CA125 was high at 350 IU / ml. Surgical exploration by laparotomy was indicated, highlighting two tumor ovaries, several peritoneal implants and significant ascites. A total non-conservative hysterectomy associated with an omentectomy with maximum reduction of peritoneal implants were performed. Anatomopathological analysis of the surgical specimens showed a histology and an immunohistochemical profile in favor of mammary lobular adenocarcinoma. Weekly paclitaxel + Trastuzumab-based chemotherapy was indicated postoperatively.

## DISCUSSION

### Epidemiology

Ovarian metastases account for 5.2 to 10% of all ovarian neoplasias.<sup>[2,3]</sup> Breast neoplasia accounts for nearly 30% of these adnexal metastases.<sup>[4]</sup>

In addition, the frequency of ovarian metastases in breast cancer patients is varied according to the authors and the type of series, with figures ranging from 13.2 to 37.8%.

Lobular carcinoma of the breast shows topography for the pelvis and appendages as a metastatic site compared to ductal carcinoma,<sup>[5]</sup> which is consistent with our study: 2 out of 3 patients had lobular carcinoma.

The discovery of a suspicious adnexal mass in a patient with a history of breast cancer poses the following problem: is it a primitive ovarian neoplasia or a metastasis of breast cancer?

The two diagnoses responding to different therapeutic strategies, it is necessary to be able to differentiate them. The probability of primary ovarian cancer is three times higher than that of an adnexal metastasis of breast cancer.<sup>[6]</sup> The probability of metastasis, however, increases with the initial staging of breast cancer. Thus, in case of discovery of an adnexal mass in a patient with metastatic breast cancer, the probability is reversed with seven times more adnexal metastasis than primary ovarian cancer.<sup>[7]</sup>

In a series of 82 ovarian metastases, Petru et al. found in 28 patients a primary breast cancer (34%). Similarly, Demopoulos et al., in a retrospective series of 96 ovarian metastases, found a mammary origin in 32 cases, or about a third of the total number of these ovarian metastases.<sup>[8]</sup>

### Histological features of metastatic ovaries

#### In macroscopy

The macroscopic appearance of the metastatic ovary is usually that of a solid tumor. Ovarian metastases, particularly of mammary origin, are usually small and the frequency of microscopic metastases varies between 24 and 31%<sup>[8,9]</sup> In the Gagnon et al. Study, the appearance of the ovary was normal in 46% of cases and only 15% of metastases exceeded 5 cm.<sup>[10]</sup> In addition, metastatic disease is in more than half of cases bilateral.

#### In microscopy

The cellular architecture of ovarian metastasis of breast cancers also varies according to the cellular type of the primary tumor. Thus, neoplastic cells derived from infiltrating lobular carcinomas (CLI) more readily infiltrate the ovarian stroma in a diffuse manner, in contrast to infiltrating ductal carcinoma cells which more readily result in the constitution of sufficiently individualizable tumor nodules<sup>[11]</sup> Several explanations have been proposed to understand this particularity of the CLIs: fibronectin deficiency on the epithelial border of the cells thus decreasing the adhesiveness of the cells and thus facilitating the infiltration, deficiency in certain molecules involved in cellular adhesion such as cadherin D.<sup>[12]</sup>

### Diagnosis and screening

Ovarian metastases, when they are small, are most often unrecognized and accidentally discovered.<sup>[10]</sup> This asymptomatic nature raises the problem of the desirability of a systematic screening policy by pelvic ultrasound or the determination of tumor markers during the surveillance of treated breast cancer.

### Clinical signs

The average age of patients at diagnosis of ovarian metastasis varies little according to the studies and is in the first half of the fifties. More interesting to consider is the interval between the diagnosis of primary cancer and that of ovarian metastasis.<sup>[12,13,14]</sup> This delay is very variable depending on the studies, ranging from 11.5 months for Gagnon et al. at 63 months in the series of Bouëdec et al.<sup>[10,13]</sup> In the study, the average time was 30 months.

Since ovarian metastases rarely exceed 5 cm, they are rarely caused by compressive disorders. When clinically speaking, ovarian metastases are often in the stage of peritoneal carcinomatosis.

In our study only one patient was symptomatic.

### Imagery

Endovaginal ultrasound is the test of choice for ovarian mass diagnosis.<sup>[12]</sup>

Similarly, systematic routine ultrasound monitoring does not seem desirable once breast cancer is treated. This, because of a high rate of false positives, would lead to an unacceptable rate of surgical checks. Only when clinical signs appear on gynecological examination should an ultrasound assessment be undertaken. For Le Bouedec et al., This examination also appears essential in view of any isolated elevation of biochemical markers and in particular of CA15-3.<sup>[13]</sup>

### Biology

Antigenic markers such as CA15-3 and ACE are widely used in routine practice for the progressive follow-up of the disease in women with breast cancer. The value of these markers in screening for metastatic recurrence remains low sensitivity. Similarly, CA 125, the usual marker for epithelial ovarian cancer, seems insensitive for screening for ovarian breast cancer metastases.<sup>[12,13]</sup>

The CEA assay is significantly higher in case of adnexal metastases, but is also high in nearly 20% of primary ovarian cancers.<sup>[3]</sup>

These different elements (imaging and medical biology) do not allow to make a diagnosis, the surgical exploration is essential, and the confirmation is anatomopathological.

### Therapeutic care

In the case of a history of breast cancer, laparoscopy will provide the necessary biopsy specimens for histological diagnosis, as well as an accurate evaluation of the abdominal extension and the resectability of the metastatic lesions, possibly avoiding unnecessary laparotomy in the case of breast cancer. a benign adnexal process.<sup>[1,7]</sup> This laparoscopic surgery must meet the same requirements as those for the treatment of a primary tumor of the ovary.

There is no consensus when defining optimal surgery. It seems that the benefit in terms of survival depends on the postoperative tumor residue. Median survival in the presence of a tumor residue  $\leq 2$ cm tends to be significantly higher than in the presence of tumor residue  $\geq 2$ cm.<sup>[2]</sup>

### Prognosis

The prognosis of patients with metastatic breast cancer at the ovarian level is very poor with survival at 5 years between 26 and 44%.<sup>[1,4,15]</sup> Eitan et al. showed a trend towards improvement in terms of survival for patients who had optimal abdominal debulking (54 months of median survival after optimal debulking versus 21 months following surgical debulking leaving tumor residues  $> 2$  cm). The time to onset of adnexal metastases also seems important: the longer the interval between the

diagnosis of breast cancer and the onset of pelvic metastases, the better the survival of these patients.<sup>[16]</sup>

### CONCLUSION

The adnexal metastases of breast cancer are often the manifestation of metastatic progression in a patient with a known history of breast cancer but may more rarely be the initial manifestation. Medical imaging is not very discriminating to establish the diagnosis of metastatic adnexal mass. In the case of a history of breast cancer, laparoscopy seems to be the preferred route of investigation for establishing histological diagnosis and assessing the resectability of lesions. It appears that complete excision of abdominal metastases may provide a survival benefit to these patients as long as there has been a free interval of at least five years since the initial diagnosis of breast cancer.

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