

Uterine metastases from breast cancer – literature review

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ABSTRACT

Uterine metastases from extragenital cancers in the absence of associated ovarian metastases represents a very scarce event, isolated cases being reported so far. The aim of the current paper is to discuss about this issue and to present the most relevant cases presented so far from the point of view of positive and differential diagnostic and of the most appropriate therapeutic strategy. Meanwhile attention on the impact on the overall survival was focused.

Keywords: uterine metastases, breast cancer, hematogenous spread, survival

INTRODUCTION

Due to the wide implementation of screening programs for early detection of breast cancer worldwide, this gynecologic malignancy has been detected in earlier stages of the disease in the last decade and therefore, the overall prognostic is significantly improved [1]. Meanwhile, discovering new chemotherapeutics and immunotherapeutic agents in association with the wide implementation of the concept of personalized medicine led to a significant increase of the overall survival of breast cancer patients even in cases in which the diagnostic is established in more advanced stages of the disease or in cases in which biologically aggressive tumors are encountered [2,3]. However, in certain cases, despite all these progresses, there are still cases when disseminated, distant metastases occur, the most commonly affected organs being represented by lung, liver, ovary and bone [4-7]. Among less com-

mon sites of metastatic involvement, the uterine body and cervix are cited, these organs being frequently affected if ovarian metastases are present [8].

CLINICAL SYMPTOMS

As expected, the most commonly encountered symptom in cases diagnosed with uterine metastases is represented by uterine bleeding; in such cases, especially if hormonal therapy had been administered for breast cancer, the first diagnostic to be excluded is the one represented by endometrial hyperplasia/endometrial cancer [8,9]. However, it seems that the previous history of hormone therapy such as Tamoxifen administration is related not only to a higher risk of endometrial cancer development but also to the apparition of modifications of the uterine environment creating therefore the premises for uterine metastases [9-12]. In the study

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conducted by Bouvier et al. which reviewed 44 cases diagnosed with uterine metastases from breast cancer the authors underlined the fact that 66% of cases were investigated for uterine bleeding at the time when the diagnostic of metastatic disease was established while other 18% remained asymptomatic [9]. As expected, most often uterine metastases from breast cancer were metachronous lesions. In cases in which the metastatic lesions are developed at the level of the myometrium, unspecific symptoms such as diffuse abdominal pain can be encountered [10].

When it comes to the characteristics of the breast lesions which are most frequently associated with uterine metastases, it seems that larger dimensions, local extension to the chest wall, lobular subtype and positive axillary lymph nodes are most commonly associated with the risk of developing uterine metastases.

PARACLINICAL TESTS

When it comes to the paraclinical tests which might provide a positive diagnostic of metastatic disease, we should underline the fact that if the metastatic lesion does not have expression at the level of the endometrial lining, the hysteroscopy and the endometrial biopsy will fail to establish the diagnostic [9]. Meanwhile, cases in which metastatic disease is present at the level of the endometrial lining attention should be paid to the fact that the endometrial lining per se will not present any sign of proper tumoral transformation or endometrial hyperplasia. In the meantime, the presence of breast antibodies such as GCDFP-15 will orientate the final diagnostic [13].

THERAPEUTIC STRATEGIES FOR UTERINE METASTASES FROM BREAST CANCER

As mentioned before, most often uterine metastases from breast cancer represent the sign of a systemic spread of the disease and is usually associated

with other hematogenous metastases; therefore, in such cases systemic treatment by the means of chemotherapy represent the first intent option. Meanwhile, in cases in which uterine metastases are found as oligometastatic disease or if systemic response is observed, surgery might be taken in consideration with promising results [9].

According to Bouvier's review, total hysterectomy with bilateral adnexectomy is the option of choice in the setting of oligometastatic disease, this procedure being performed in 57% of cases. Another extremely interesting aspect which was pointed out in the above mentioned paper was the fact that in four out of 44 included cases a pelvic lymph node dissection was associated and in three of them metastatic lesions were found, therefore demonstrating that both the hematogenous and lymphatic routes had been incriminated in the process of metastasizing of the initial breast tumor. As for the long-term outcomes, the same study underlined the fact that the overall survival remains poor, in the cases included in their paper the median overall survival from the time of uterine metastases diagnostic being of only 14 months; as expected, cases presenting unique uterine metastases reported a significantly longer survival when compared to cases presenting multiple lesions (22 months versus 10 months) [9].

CONCLUSIONS

Although represent rare eventualities, uterine metastases from breast cancer can be encountered; this diagnostic should be kept in mind whenever a patient with previous history of breast cancer presents abnormal vaginal bleeding or any suspect mass at the level of the uterine body. Although these lesions are usually found in association with ovarian cases, in scarce cases isolated uterine metastases might be encountered. As for the therapeutic strategy, it varies between systemic therapy and excision (usually through total hysterectomy en bloc with bilateral adnexectomy) the final decision being taken accordingly to the extent of metastatic disease.

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REFERENCES

- Desantis C, Ma J, Bryan L, Jemal A. Breast cancer statistics, 2013. *CA A Cancer Journal for Clinicians*. 2014;64:52–62.
- Hudis CA. Trastuzumab—mechanism of action and use in clinical practice. *New England Journal of Medicine*. 2007;357:39–51.
- Huang HJ, Neven P, Drijkoningen M et al. Association between tumour characteristics and her-2/neu by immunohistochemistry in 1362 women with primary operable breast cancer. *Journal of Clinical Pathology*. 2005;58:611–616.
- Verma R, Bowen RL, Slater SE et al. Pathological and epidemiological factors associated with advanced stage at diagnosis of breast cancer. *British Medical Bulletin*. 2012;103:129–145.
- Gerratana L, Fanotto V, Bonotto M et al. Pattern of metastasis and outcome in patients with breast cancer. *Clin Exp Metastasis*. 2015;32(2):125–133.
- Blanco G, Holli K, Heikkinen M et al. Prognostic factors in recurrent breast cancer: relationship to site of recurrence, disease-free interval, female sex steroid receptors, ploidy and histological malignancy grading. *Br J Cancer*. 1990;62(1):142–146.
- Metzger-Filho O, Sun Z, Viale G et al. Patterns of Recurrence and outcome according to breast cancer subtypes in lymph node-negative disease: results from international breast cancer study group trials VIII and IX. *J Clin Oncol Off J Am Soc Clin Oncol*. 2013;31(25):3083–3090.

8. Piura B, Yanai-Inbar I, Rabinovich A et al. Abnormal uterine bleeding as a presenting sign of metastases to the uterine corpus, cervix and vagina in a breast cancer patient on tamoxifen therapy. *European Journal of Obstetrics, Gynecology and Reproductive Biology*. 1999;83(1):57-61.
9. Bouvier AS, Panchbhaya N, Brochard C et al. Uterine metastasis from invasive ductal breast carcinoma: A case report with literature review. *J Gynecol Obstet Hum Reprod*. 2021;50:101993.
10. Kumar NB, Hart WR. Metastases to the uterine corpus from extragenital cancers. A clinicopathologic study of 63 cases. *Cancer*. 1982; 50(10): 2163–2169.
11. Lee S, Kim YH, Kim SC et al. The effect of tamoxifen therapy on the endometrium and ovarian cyst formation in patients with breast cancer. *Obstet Gynecol Sci*. 2018;61(5):615–620.
12. Holmes CE, Huang JC, Pace TR et al. Tamoxifen and aromatase inhibitors differentially affect vascular endothelial growth factor and endostatin levels in women with breast cancer. *Clin Cancer Res*. 2008;14 :3070–3076.
13. Fiel MI, Cernaianu G, Burstein DE, Batheja N. Value of GCDFP-15 (BRST-2) as a specific immunocytochemical marker for breast carcinoma in cytologic specimens. *Acta Cytol*. 1996;40(4):637-641.