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Metastatic Breast Cancer to the Cervix: A Case Report and Literature Review

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Abstract:-
Background: Breast cancer is the first female cancer in Morocco and worldwide. The most common metastatic sites in breast cancer are the liver, bones, lungs and, less frequently, the brain. Metastases in genital tract are very rare, thus the literature reported a few cases.

Case report: A 56 years old women, with family history (two sisters followed for breast cancer, a mother died of leukemia and the father died of liver cancer), was followed since 2007 for locally advanced and non-metastatic breast cancer, she was treated initially by upfront chemotherapy then a total left mastectomy with homolateral axillary lymphadenectomy and then hormonotherapy (Tamoxifene). The follow up of our patient reveals multiple metastatic sites including the site of mastectomy, lymph nodes, the bone and a rare site wich is the uterine cervix. We are reporting this case to alert our hospital practitioners to the possibility of this association and the need for a full gynaecological examination and eventually a biopsy for all breast cancer patients.

Conclusion: Any genital bleeding that occurs during the follow-up of patients on breast cancer's traitement should not be routinely linked to hormonotherapy. Our case draws our attention to the importance of gynaecological examination as part of breast cancer follow-up in order to detect metastases in the genital tract, even if they are extremely rare.

Keywords:- *Breast Cancer, Vaginal Bleeding, Cervix, Metastasis, Follow-Up.*

I. INTRODUCTION

Breast cancer is the most frequently diagnosed cancer worldwide and is the leading cause of cancer death in women [1]. The mortality rate has been significantly reduced through several screening programs and the promotion of treatment of primary tumors. However, the clinical management of patients with metastatic progression is much less well structured.

Metastases of the female genital tract from extra-genital origin are infrequent, and about 4% of all tumors. The frequency of cervical metastases in breast cancer is much rarer, estimated at between 0.8% and 1.7% [2], and only 35 cases have been reported in the literature. At the time of diagnosis none of these metastases were synchronous from the primary tumor [3].

We present the case of a patient undergoing chemotherapy for breast cancer with discovered metastases in the cervix.

II. CASE REPORT

The following case is about a 56-year-old woman, who is menopaused since 12 years, cholecystectomized in 2014 and multigravida; a family history revealed: two sisters followed for breast cancer, a mother died of leukemia and the father died of liver cancer.

Our patient was Followed since 2007 for locally advanced and non-metastatic left breast cancer; she was treated initially by upfront chemotherapy based on 06 cures of Docetaxel, and underwent a total left mastectomy with homolateral axillary lymphadenectomy.

Anatomopathological examination of the surgical specimen identified an invasive ductal carcinoma grade III of SBR, staged y PT2N1M0 with vascular emboli, the immunohistochemistry of the specimen showed positive staining for HR and negative staining for HER2.

Our patient underwent radiotherapy and tamoxifen based adjuvant hormone therapy, and was kept under clinical, biological and radiologic observation. During the follow-up, in November 2015, she presented a metastatic relapse, metastasis were identified at the site of mastectomy, lymph nodes and in bones.

Moreover, a change of the pattern of immunohistochemistry staining was identified, becoming positive for HER 2 scored at 3 (the staining stayed also positive for Hormone receptors).

Our patient received Herceptin + Letrozole, until May 2018 with radiological progression, thus she received Docetaxel + herceptin + Zometa until October 2019, when the patient presented a single episode of abnormal postcoital vaginal bleeding.

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The clinical examination revealed a patient with a performance status score of 3. As for the gynecological examination, it revealed a tumor of the cervix of 05 cm with bilateral parametrial invasion, and thus staged **IIb** of the FIGO.

A comparison of a TAP CT scan that dates back to 6 months and a recent TAP CT scan, revealed the emergence of a heterogeneous tumor process centered on the uterine cervix staged **IVa** of FIGO, with absence of endometrial thickening. A biopsy of the cervix was done with an endocervical curettage.

The anatompathological examination of the specimen showed a poorly differentiated carcinomatous process with the expression of progesterone receptors and HER2 (that was scored at 3), thereby ruling out a cervical origin to the tumor process especially since the endometrium is not thickened.

The research of the expression of the CK7, P63, GATA3 and P16 antigens was not carried out due to technical difficulties.

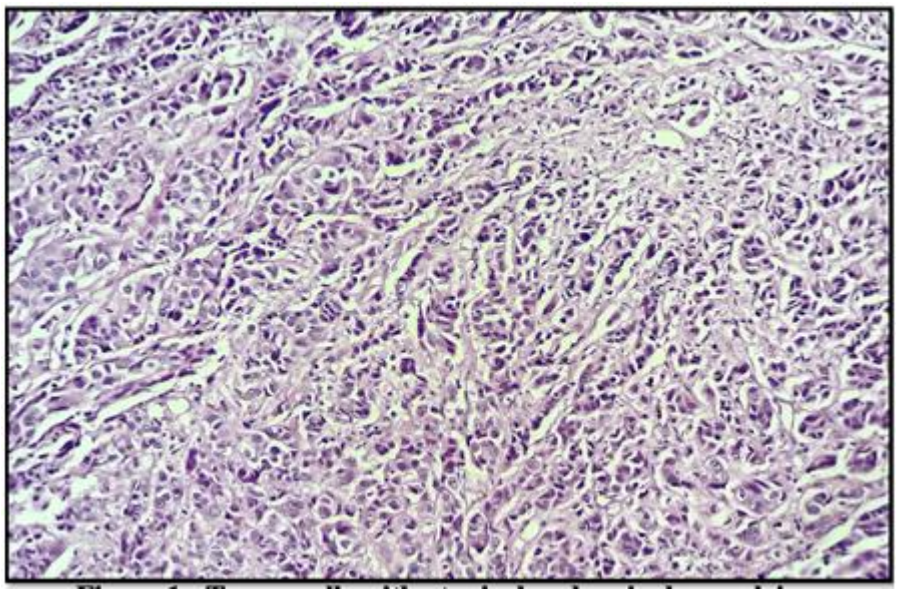

Fig 1:- Tumor cell with atypical and vasicular nuclei surrounded by a poorly defined cytoplasm (HESZ40)

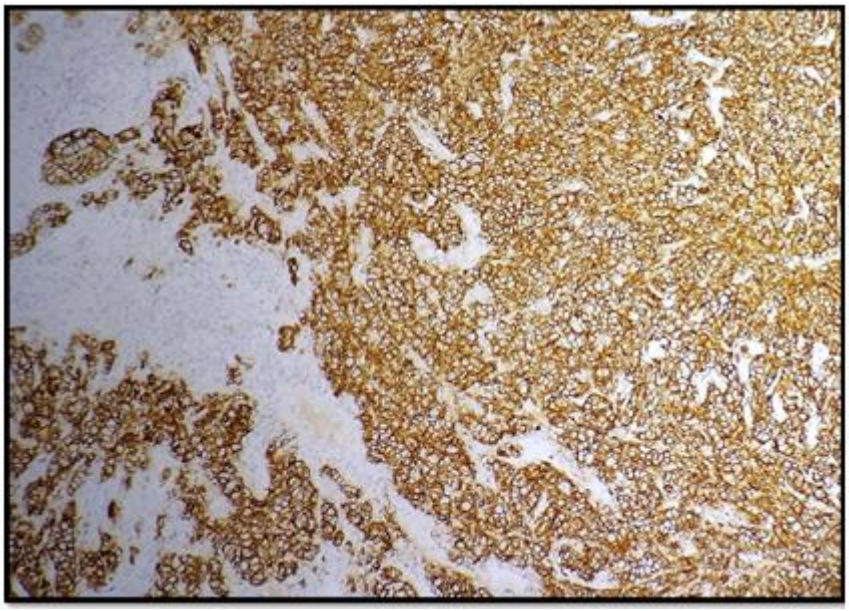

Fig 2:- Tumor cells show a strong positive staining with HER2.

For the renal failure secondary to bilateral ureteral infiltration the patient underwent bilateral nephrostomy. Unfortunately, management was limited to supportive care, given the performance score of 3, the multiple co-morbidities and the swift deterioration of the patient's clinical condition.

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III. DISCUSSION

In this paper, we report the case of a patient followed for breast cancer with the appearance, 12 years after the initial diagnosis, of lesions on the cervix. a metastatic carcinoma corresponding to the primary breast cancer was revealed bys biopsy and curettage of the cervix.

The most common metastatic sites of breast cancer are the lungs, liver and bones. The female genital tract is not frequently affected, when it is, ovarian metastases are found in 70-80% of cases. To date, approximately 35 cases of metastatic breast cancer of the cervix have been reported in the literature, with a frequency of between 0.8 and 1.7% [2]. This rarity can be explained by the fact that the cervix is a small organ with a single afferent lymphatic drainage system and limited vascularisation. Fibrous proliferation with infammatory cell response is the cervix's response to metastatic disease, which may explain the clinical outcome of an enlarged and indurated cervix [5].

It is admitted that more than 80% of metastases in gynecological organs are related to invasive lobular mammary carcinomas [6]. The reason for a different metastatic pattern between invasive lobular carcinoma and invasive ductal carcinoma is not clear: the expression of the intercellular adhesion molecule E-cadherin in infiltrating ductal carcinoma, but not in lobular carcinoma, could be responsible, at least in part, for the different metastatic spread of these tumors [6], which has been asserted by recent studies [6], thus indicating that this protein is involved in the biology of each tumor type [6], our patient had an invasive ductal carcinoma of SBR grade III.

Age plays an important role in breast cancer behavior, gynecological and liver metastases are frequently found in younger patients, our patient was 56 years old. Another factor is hormonal sensitivity, so it is the hormonosensitive subtype of invasive lobular carcinoma that metastasizes more frequently in the uterus [7].

In most cases, primary breast cancer is diagnosed before metastasis is discovered. The discovery of cervical metastasis in the first place is rare. When cervical metastases are symptomatic, vaginal bleeding is the main symptom. According to Kennebek and Alagoz [4] and Yazigi et al [2], 75% of cases of secondary cervical metastases cause vaginal bleeding, which was the case for our patient at the time of diagnosis of cervical metastasis. Other symptoms may also occur, such as vaginal discharge and lower abdominal pain.

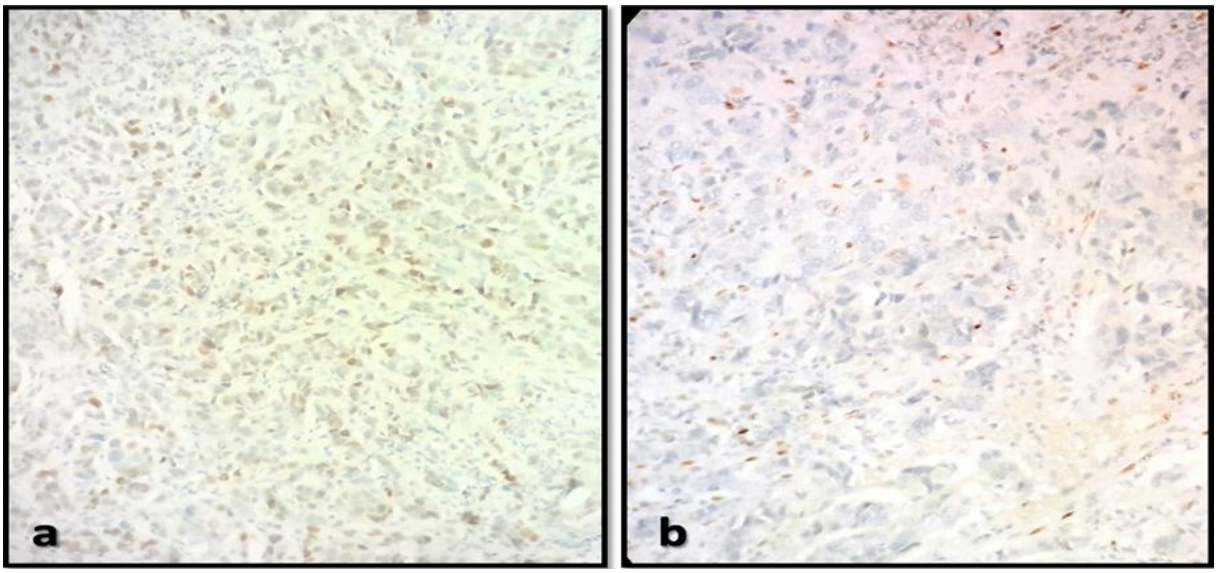

Fig 3:- Tumor cells show a weak positive staining with progesteron receptor (a), and no staining with Estrogen receptor (b)

Differentiation between breast cancer metastases and primary carcinoma of the genital tract is imperative, but difficult for several reasons: long disease-free interval, not specific symptoms, inconclusive radiological findings, and histopathology of adenocarcinoma. Immunohistological analyses, in particular staining with anti-E-cadherin, were required for differential diagnosis. The IHC (Immunohistochemistry) panel is crucial to differentiate primary cervical malignancy from metastatic cervical malignancy. Cytokeratin 7(CK7), is a type II keratin of simple non-keratinizing epithelia. The CK7+/CK20+ pattern is observed in endo-cervical cancer, and the CK7+/CK20- pattern is observed in breast, endocervical and endometrial carcinoma [7].

Gross cystic disease fluid protein 15 (GCDFP 15) is used as a specific IHC diagnostic marker for tumors originating in the breast [7]. It is a glycoprotein originally isolated in human breast gross cystic fluid.

Patients with metastatic breast disease eligible for a curative treatment strategy represent 1-3%. When metastatic disease is limited to a single operable lesion or multiple lesions at a single organ site, this curative strategy based on metastasectomy is a good treatment option [7].

Systemic or regional chemotherapy based on taxanes, vinorelbine, capecitabine, can play an important role in the therapeutic management, particularly in inoperable patients, both in terms of survival and quality of life.

Hormonotherapy (third-generation aromatase inhibitors and fulvestrant) and radiofrequency ablation can also be used.

Some patients achieve a complete response, despite the poor prognosis of this group of patients in general, and remain free of the disease for prolonged periods of time, sometimes for more than 20 years [7].

In conclusion, gynecologic and ultrasound examination of the pelvis should be an important part of follow-up investigations in women with primary breast cancer. It is also imperative to maintain a high vigilance index in all women with a history of breast cancer, and to consider metastatic involvement of the female genital tract, including the cervix, in the event of vaginal bleeding or uterine enlargement.

IV. CONCLUSION

This article emphasizes the importance of considering metastatic cancer in the differential diagnosis of abnormal vaginal bleeding. The prognosis often poor given the late diagnosis, may be better in the case of a single metastasis eligible for metastasectomy.

Conflicts of interests : Author declares no conflict of interest.

REFERENCES

[1]. ForouzanfarMH, Foreman KJ, Delossantos AM, Lozano R, Lopez AD, Murray CJ and Naghavi M: Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. Lancet 378: 1461-1484, 2011.
[2]. Yazigi R, Sandstad R, Munoz A. Breast cancer metastasizing to the uterine cervix. Cancer 1998;61:2558Y60.
[3]. Breast cancer with synchronous massive metastasis in the uterine cervix: a case report and review of the literature, DOI 10.1007/s00404-009-1264-0
[4]. Kenneberg CH, Alagoz T: Signet ring breast carcinoma metastases limited to the endometrium and cervix. Gynecol Oncol 1998;71:461–464.
[5]. bryson CA, de Courcy-Wheeler RHB, Wallace, Med J 68(1):30–32, 1999.RJ Breast cancer metastasising to the uterine cervix. Ulster
[6]. Breast cancer with synchronous massive metastasis in the uterine cervix, Stefano Bogliolo and all
[7]. Metastatic Breast Cancer to the Cervix Presenting with Abnormal Vaginal Bleeding During Chemotherapy, A Saad Abdalla Al-Zawi et all 2018 University Hospital, Essex, UK