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52-Year-Old Woman Diagnosed with Metastatic Breast Cancer Improved the Patient Disease Free Survival: Case Report

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Abstract

Metastasic Breast Cancer survival is poor, 5 years survival rate in metastasic breast cancer are 27 %.The median overall survival of these women is 2.8 years for those diagnosed at the outset, We report a case of 52-years-old woman who was diagnosis in January/ 2017 which metastasic breast cancer at the diagnosis, in this patient after several evaluations in a multidisciplinary committee in every step of a management, we used multiples arms of cancer treatment from chemotherapy , immunotherapy, to surgery of the primary tumor, This tumor presented as a locally advanced tumor ; it was negative for hormone receptor and HER 2- positive. The patient also presented bilateral pulmonary, multiple liver and bone metastases, stage IV(T4bN2M1); Treatment was composed by chemotherapy combine with trastuzumab, with simultaneous radiotherapy, which was performed over vertebral body to relief locally pain. The last twenty-one months of treatment, the trastuzumab was used as single agent. As results, the combined chemotherapy was able to eliminate the edema and erythema of the right breast besides it to decrease the ipsilateral axillary lymphadenopathy and was able to eliminate the lung metastasis; stabilized the metastases advancing in liver and vertebrae. Finally, the patient continues in treatment, it remains asymptomatic, with a small liver injury and a small abnormal activity in vertebral column. The schedule suggested in this case was efficient to improve the disease-free survival and quality of life in a patient on metastatic scenario and poor prognosis factor (bulky disease at diagnosis, 2 solid organ diseases, negative hormonal receptor, her 2 positive), who are undergoing Herceptin treatment as a monotherapy for 2 years after diagnosis (3.9 years overall survival and Eastern Cooperative Oncology Group - ECOG-2)

Introduction

Metastatic Breast Cancer (MBC) is a very heterogeneous disease whose present a poor prognosis. Generally, the metastasis in breast cancer patients is a cause-leading death. The broad understanding regarding the metastasis biology can provide a better treatment choice [1,2]. In many cases, this type of cancer present mosaics of cancer cells, which can have distinct features and different responses to therapies. When this mosaicism (distinct tumor cell populations) coexists within the same tumor specimen, but showing molecular and phenotypical differences is called intratumor (or intralesion) heterogeneity [3].

Most of breast cancer patients who were diagnosed at beginning, with metastases, have very worst prognosis. Concerning ethnicity, the African-American population that have in breast cancer present greater

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intratumor heterogeneity [4]. Additionally, that greater tumor heterogeneity tends to be associated with worse prognosis and outcome [2,5]. In triple-negative breast cancer (TNBC), the intralesion heterogeneity relating to clonal mutation, could be associated with greater chemotherapy sensitivity [6].

One well-known intratumor heterogeneity in breast cancer is relating to *erbb2* gene. This gene encodes for transdermal human epidermal growth factor receptor 2 (HER2) [7]. The *erbb2* gene is amplified and/or overexpressed in approximately 20% of breast cancer patients [8]. Drugs that target the HER2 receptor have transformed outcomes for patients with *erbb2* amplified (HER2- positive) breast cancer [7]. Recurrent somatic mutations of *erbb2* are identified in 2% to 4% of patients [9].

Determining the breast cancer subtype based in patterns of intertumoral heterogeneity allows evaluating its natural history and determining specific treatments [2]. The HER2+ subtype (with overexpression HER2 or amplification of its gene) is characterized by aggressive evolution and worse prognosis in the absence of treatment [10]. In this subtype, management based on chemotherapy with anti-HER2 agents has changed its evolution, improving disease-free survival as well as overall survive (OS) [11]. Although, in the past decade, the overall survival has improved dramatically in HER2-positive MBC patients, it remains higher for *de novo* MBC than relapsed disease [12]. Other challenges continue, including *de novo* and acquired resistance to HER2-targeted antibody therapy [13]. Furthermore, the efficacy of pertuzumab or T-DM1 in MBC is unknown, even after adjuvant treatment with either mentioned agent. Few agents have demonstrated activity in reducing the incidence of central nervous system metastases [14]. Although central nervous system recurrence is a particular challenge in breast cancer [15,16]. The median overall survival of these women is 2.8 years for those diagnosed at the outset as our patient

Clinical Case

A 52-year-old woman has been diagnosed with breast cancer since january/2017. A core biopsy showed invasive ductal carcinoma with moderate differentiation associated with mixed carcinoma *in situ*, a cribriform and comedocarcinoma, nuclear grade 2, negative hormone receptor, HER2 -2 (amplified by FISH). At the time, TAC-extension studies revealed bilateral pulmonary metastases and multiple liver metastases. The analysis of bone scintigraphy showed an increase in the main activity of the dorsal spine in the D8-D9 vertebrae, compatible with bone metastases. A multidisciplinary committee evaluated the case and decided to start with palliative chemotherapy. At the time of diagnosis, physical examination showed a notable erythema affecting the entire right breast, associated with edema and ipsilateral axillary adenopathy in her right supraclavicular pit. Clinically, her tumor was classified as T4b N3M1. FAC (5 Fluoracil 750 mg, Adramycin 75 mg and Cytoxan 750 mg) was used for four cycles. After that period, four cycles of paclitaxel (120 mg) combined with trastuzumab + zometa were performed. A new control TAC-extension studies was done and it showed no variation from that of admission time.

After bone gameography, focal hyper capture was observed in dorsal vertebrae and left iliac bone. The multidisciplinary committee decided to continue with trastuzumab as single agent, and ten months later, the tests were repeated. Bone scintigraphy showed stability of vertebral lesions without signs of metastasis of the iliac bone. TAC results demonstrated stable liver disease and no lung disease. At this point of the treatment, the patient underwent radiotherapy in the L-1 dorsal spine; for focal symptoms. Thus, treatment with trastuzumab as single agent was continued for another eleven months. A new CT scan of this patient reported only an expansive process of the right breast and a small image of a 13 mm liver lesion. A new bone scan showed no apparent injury in the dorsal spine. Therefore, the multiprotection committee chose to perform the surgery due to the good response of patient disease. The patient was authorized to perform this procedure, which was operated on 12/17/2019. The surgical procedure performed a total mastectomy + right axillary dissection.

The operative biopsy reported invasive ductal carcinoma, poor differentiated and a maximum tumor size of 4 cm. In addition, this sample presented a positive lymph vascular invasion, a positive tumor necrosis, without skin involvement and a high-grade ductal component of *in situ* type with a 0.7 c of diameter. Regarding metastasis, metastasis was found in 1/7 lymph nodes without extra capsular involvement. therefore, ypT2N1 M1 stage.

Last CT scan showed no remote disease, stable liver injury of 12 mm size. The last bone scintigraphy presented abnormal osteoblastic activity of D8-D9 vertebrae. Radiant treatment was performed in the vertebral area for treatment of dorsal pain. Currently, the patient continues under treatment with herceptin in doses of 50 mg. The patient remains asymptomatic for breast cancer (ECOG-2)

Discussion

Treatment in metastatic stage is focus on improve life quality and to relief the symptoms. Several managements can be prescribed for metastatic patients, which need consider the site of metastases diseases, number of metastatic sites, age of the patient and symptoms. This previous study in each case makes it possible for oncologist to adjust individual patient treatment. Metastatic breast cancer includes two types of patients: patients diagnosed with cancer who presents metastasis at the time of being diagnoses (de novo) and patients who progressing after having had an early stage (I to III). The incidence of de novo metastatic breast cancer diseases is 5% in worldwide. Additionally, 6% of patients with local relapse present metastasis and 30% develop remote metastasis during the course of their disease [17-19]. Generally, metastatic breast cancer is incurable and the 5 years survival is about 20.1% [20]. There is no consensus if patients with de novo metastasis have worse survival than those in relapse. Dawood et al. (2010) [21] found that the survival of patients depends on the time of relapse. The survival of the de novo metastasis patients is similar to those

patients who present relapse after 24 months of diagnosis, better than those who turn to have tumor again less than 24 months after diagnosis or who received adjuvant chemotherapy. However, the survival of them is worse than those who present relapse after five years. Zeichner et al. (2015) [22] found a greater survival in de novo patients than those reported by Dawood and colleagues (2010). It is important to consider that perhaps the findings of this study population having different racial characteristics implying in the results, although they do not claim or refute that survival is better than that of mentioned patients. Chia et al. [23] found no difference in survival between de novo cancer patients and those who present relapse event within the first five years of their initial diagnosis. Additionally, co-expression of hormone receptors and oligometastatic disease have been associated with increased overall survive in patients with metastatic breast cancer, HER2-positive, it presenting high histological grade, in the stage III, with less than 2 years relapse free disease. In addition, liver engagement have been with a shorter overall survive time [24-26]. Liver metastases from breast cancer are the second most common site of metastases and occur more often among people with HER2-positive tumors [27]. Lung metastases from breast cancer are treated primarily with general measures to treat the breast cancer, such as hormonal therapies, HER2-targeted drugs, and chemotherapy, rather than any specific treatments. In a metastatic study, a pivotal phase III trial was compared to first-line chemotherapy (doxorubicin/epirubicin and cyclophosphamide or paclitaxel) plus trastuzumab versus chemotherapy alone in HER2-positive patients. Trastuzumab plus chemotherapy was associated with a significant improvement in time to disease progression (7.4 mo vs 4.6 mo), objective response rate (50% vs 32%), and 1-year survival (25.1 mo vs 20.3 mo) compared with chemotherapy alone. [28] When breast cancer is metastatic at the time of diagnosis, surgery has not usually indicated, once it was believed that surgery could not did not improve patient's survival rates. This thought appears to be changing, with evidence that primary surgery in people with breast cancer, stage IV and HER2-positive can improve the overall survival. In addition, when a breast tumor is causing symptoms (if it is painful, bleeding, draining, or becomes infected), palliative mastectomy may significantly reduce symptoms. Palliative mastectomy was found to improve quality of life for some people [29]. We take a calculated risk with the agreement of patient to carry out surgery as local treatment, due her positive response to trastuzumab and chemotherapy.

Conclusion

A 52-years-old woman was diagnosis with breast cancer metastatic at the time of diagnosis, also it presented negative for hormone receptor and HER2 -2 positive, besides bilateral pulmonary, multiple liver and bone metastases (vertebrae and iliac bone). In addition, the patient presented in the completely right breast a notable erythema. As metastatic breast cancer are incurable tumors, it was offered palliatives treatment to improve the overall survival of the patient as well as improve her quality life. Several palliatives treatment schedules and surgery (total mastectomy + right axillary dissection) were performed in the patient. The treatment composed of four FAC cycles and after, four cycles of docetaxel and trastuzumab with simultaneous radiotherapy over L1-L2 vertebral body was able to eliminate the edema and erythema of right breast. However, the metastases scenario in lung, liver and bone remained. Then, the patient during was submitted for 11 months to trastuzumab treatment as single chemotherapy agent. At time, our schedule using trastuzumab as single chemotherapy was able to eliminate the lung and the iliac bone metastases besides to stable the liver and vertebral metastasis. These good results made possible the palliative surgery (total mastectomy + right axillary dissection). The treatment of patient is ongoing more than 13 months ago, it remains asymptomatic for breast cancer after surgery, with a small liver injury and a small abnormal activity in vertebral column. Our palliative schedule could be efficient to improve the overall disease-free survival of metastatic breast patient with pulmonary, liver and bone metastases, who had a good ECOG, and her 2-positive cancer.

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