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Case Report

Metastatic Triple-Positive Breast Cancer: A Case Report Not Response to Standard Protocols and Still Alive

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Abstract

Breast cancer is the most common female cancer, the second most common cause of cancer death in women, and the main cause of death in women ages 40 to 49 years. Metastatic breast cancer is breast cancer that has spread beyond the breast and nearby lymph nodes to other parts of the body (most often the bones, lungs, liver or brain). The heterogenicity of Breast Cancer (BC) is determined by the status of human epidermal growth factor receptor 2 (HER2/neu), Estrogen Receptor (ER), and Progesterone Receptor (PR), Triple-Positive BC (TPBC). Human Epidermal Growth Factor Receptor 2 (HER2) is overexpressed and/or amplified in approximately 20% of breast cancers, HER-2 positivity is commonly associated with a more aggressive tumor phenotype and decreased overall survival and, moreover, with a reduced benefit from endocrine treatment. Our case is a Metastatic breast cancer with Triple positive, not response to standard protocols but she is still alive since seven years with minor complain until now.

Keywords: Metastatic breast cancer; Human epidermal growth factor receptor 2 (HER-2neu); Triple positive

Introduction

Breast cancer is the most common malignancy in women worldwide (One every 9 women is statistically involved.). About 13% of American women are afflicted with breast cancer, with the mortality rate of 3% [1]. Most patients with overt distant metastases are presently incurable [2].

About one-third of women diagnosed with metastatic breast cancer in the U.S. live at least 5 years after diagnosis [3]. Over the past four decades, systemic therapy with endocrine therapy or cytotoxic chemotherapy became the fundamental treatment approach of the management of metastatic breast cancer [4].

HER2-positive (HER2+) breast tumors are more aggressive and historically have been associated with poorer outcomes compared to HER2-negative (HER2-neu) tumors [5]. Subsequent data show that the addition of trastuzumab to adjuvant chemotherapy results in durable survival benefits for patients with HER2-positive breast cancer [6].

Today, there is no clear therapeutic algorithm for patients with metastatic HER2-positive breast cancer who have progressed to trastuzumab, pertuzumab, and T-DM1. Some women may live 10 or more years beyond diagnosis [7]. In this article, we exposed a case of Metastasis breast cancer with Triple positive, not response to standard protocols but she is still alive with minor complain until publish this article.

Case Presentation

The patient was a 53-year-old post-menopausal female, who initially palpated a lump in her left breast, diagnosed by FNAC, otherwise an unremarkable medical history, she had no cancer history in her family. She underwent left Mastectomy (MRM) and axillary lymph node dissection in late 2012. Histopathology result was IDC, Lymph nodes are positive, Immunohistochemistry (IHC) was Estrogen Receptor (ER) and Progesterone Receptor (PR) positive and HER2 positive which called Triple positive. Following completion of adjuvant chemotherapy 4AC plus 4Paclitaxel without Herceptin, because it was not available in our country at that time, then she completed standard adjuvant radiation therapy, after that She started on Tamoxifen. The patient was well until approximately 1.5 years (July 2014) after the initial diagnosis. On 2014 when we were doing the routine follow up appeared by Chest-CT scan; nodule in her Lung about 1.5x1 cm, not present previously. Her Karnofsky performance status was one, without any complain. BSA was 1.7m^2, Abdomen and pelvic ultrasonography was normal but the Tumor markers were very high, CA15.3:300, CEA: 6.5. Ejection Fraction of her heart was 65%. We gave her tamoxifen with Capecitabine orally with evaluation every three months. She well tolerance with good response and disappear the Chest nodule and Tumor markers return to normal value. After that patient was on follow up until January 2017 recurrence the chest nodule and elevated the Tumor markers again, patient given Trastuzumab with Docetaxel, after the three cycles were no more response, we shifted to Trastuzumab with Capecitabine, patient was stable for several months but the tumor markers are elevated CA15 >300, CEA >10, patient given Lapatinib with Capecitabine, no response paraclinical, we changed to Trastuzumab with lapatinib to reaching to more effect and more response. She was stable, until appeared pleural effusion on late 2017, we gave her paclitaxel protein-bound (Abraxane) 400mg every three weeks, we reached to accepted response, we put the patient on Letrozole alone. On September 2018 during evaluation there were progression appeared by multiple bone lesions with pleural thickening, patient received Lapatinib with Aramidex orally, no any response, we changed to Gemcitabine D1,8 plus Carboplatin D1 every three weeks with Zoledronic acid

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(Zometa) monthly, the response was excellent. Unfortunately at the end of 2019 our case was progressed through the routine evaluation, CT-scans were; multiple sclerotic bone lesions plus multiple pleural &pulmonary nodules in Rt lung only, CEA:7.5, CA15.3>300. Fortunately, no any complain. Patient received Trastuzumab plus Navelbine with Zometa. The patient continued to do well until a follow up brain MRI on June 2020 demonstrated a new Brain metastasis. She received Cranial Irradiation by Cyberknife machine and palliative Radiotherapy for some painful Bone areas. Then she given Ado-trastuzumab emtansine, post three cycle evaluated by PET-CT-scan; no more response were seen. She shifted to Gemzar D1,8 plus Erobulin D1,8 every three weeks with Zometa monthly ,patient was stable until finished six cycles. She was on follow up. Last evaluation was done on June 2021 by CT scans appeared some progression in bone metastasis and small nodules in lungs without any complain with elevation in Tumor markers, CEA:17, CA15.3 >300, patient given Navelbine tab d1,8 a single agent orally and she is stable until publish this article.

Discussion

Metastasis occurred in 27.4% of the cases, a study by Kennecke H et al. stated that Triple Positive Breast Cancer (TPBC) had the highest tendency of metastasis among the other molecular subtypes [8]. HER-2 protein overexpression or gene amplification is reported in 15-20% of primary breast carcinomas and is associated with decreased Disease Free Survival (DFS) and Overall Survival (OS) [9]. TPBC has a higher grade, larger size, and worse prognosis when compared to triple-negative BC (Ades et al. 2014) [10]. HER2-positive tumors that are also ER-positive (triple-positive), however, may behave more like ER-positive tumors and HER2-negative tumors, being less aggressive and more responsive to hormonal treatment [11]. The optimal therapy sequence remains unclear [12]. Regard to treatment, it is commonly believed that HER-2 blocking agents are effective in patients with HER-2-positive disease, irrespective of HR status [13]. CA15-3 may be helpful in determining the extent of the spread of breast cancer. The bone scan was assumed as a gold standard [14]. In some cases, blood tests for tumor markers may be used to help monitor metastatic breast cancer [15]. The CA15-3 tumor marker has been widely considered for the prognosis of bone metastases in patients with breast cancer [16]. PET scanning might serve to differentiate malignant from benign solitary lesions, and might also be useful in monitoring response to therapy [17].

Recent ASCO guidelines still recommend as first line treatment for advanced breast cancer the combination of HER-2 blocking agents and chemotherapy as the optimal choice, but also consider the use of endocrine treatment combined with HER-2 target therapy [18]. HER2-positivity in HR-positive disease is associated with endocrine resistance. Cross-talk between the two pathways exists, and inhibition of HER2 pathway seems to restore hormone sensitivity [19]. In particular, approximately 50% of patients with stage IV, HER2 positive breast cancer experience metastatic disease in the brain at some point of their disease refractory [20]. Stopping anti-HER2 therapy may be considered in highly selected patients, particularly if treatment rechallenge is available in case of progression [21]. Adding tucatinib, neratinib or lapatinib to treatment may give women who have HER2-positive metastatic cancer with brain metastases more time before the cancer spreads [22]. The structure of skeletal system is more attractive to metastasis homing because of hematopoietic activity due to high perfusion and growth factors [23]. Osseous metastases represent the commonest type of metastatic spread in breast cancer during the clinical course of the illness [24].

Conclusion

Metastatic breast cancer is breast cancer that has spread beyond the breast and nearby lymph nodes to other parts of the body (most often the bones, lungs, liver or brain). As hard as it is to hear, metastatic breast cancer cannot be cured today. However, metastatic breast cancer can be treated. Treatment focuses on extending life and maintaining quality of life. BC should always be approached according to the status of its receptors and emphasis should be given to the early diagnosis and treatment of TPBC to prevent the morbidity and mortality associated with its tendency for early metastasis. Our case is a Metastastic breast cancer with Triple positive, not response to standard protocols but still alive for more than seven years until publish this article.

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