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Case Report
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Complete Response of a Leptomeningeal and Brain Relapse Following Treatment with Pertuzumab Plus Trastuzumab Plus Paclitaxel of a HER2 Positive Breast Cancer

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Abstract

Central nervous system and leptomeningeal disease due to HER2-positive breast cancer has limited treatment options and poor prognosis. A 67-year-old female previously treated because of a localized HER2-positive breast cancer presented to the Emergency Department in December 2019 due to a 3-month history of worsening headaches and diminished sensation in the left facial area. A Magnetic resonance of the brain demonstrated four intracranial lesions and leptomeningeal disease suggestive of disseminated disease. Pertuzumab 840 mg IV day 1 followed by 420 mg and trastuzumab 8 mg/kg IV on day 1 followed by 6 mg/kg IV cycled every 21 days, and weekly paclitaxel 75 mg/m^2 IV was performed for 9 months. Clinical and radiological response was achieved and maintained for more than 34 months.

Introduction

Brain metastasis occurs in one third of HER2 positive metastatic breast cancer patients [1]. The management of Central Nervous System (CNS) metastatic disease includes surgery, radiotherapy and systemic anticancer therapies. Few clinical trials have evaluated the effectiveness of systemic therapies for HER2 positive disease on brain metastasis. Furthermore, evidence of leptomeningeal disease response on systemic therapies is limited.

Case Presentation

A 67-year-old woman presented to our Medical Oncology Department in March 2020 following an intracranial relapse of her breast cancer. Her past medical history included major depression treated with escitalopram in 2010. Her last menstrual period was in 2008.

She was diagnosed with a ductal carcinoma of the right breast in 2016 in a public hospital in Spain. The tumor was located in the inferior-external quadrant and its larger diameter was 5 cm, 8 cm on breast ultrasound, with no lymphatic involvement. A CT scan excluded metastatic disease. Clinical stage was cT3N0M0. Immunohistochemistry showed no estrogen or progesterone expression, a positive staining of HER2 (3+) and an expression of Ki 67 in 30 % of the tumor cells.

She received neoadjuvant treatment with combination systemic therapy. First, epirubicin 90 mg/m^2 and cyclophosphamide 600 mg/m^2 were administered every 21 days for four cycles. Subsequently, the patient received treatment with paclitaxel 75 mg/m^2 IV weekly, trastuzumab 8 mg/kg day 1 IV, followed by 6 mg/kg IV and pertuzumab 840 mg IV followed by 420 mg IV, cycled every 3 weeks for 12 courses. Total mastectomy and sentinel lymph node biopsy was performed and the pathology report showed pathological complete response (ypT0ypN0sn).

Adjuvant radiotherapy was planned to the thoracic wall and to the axillary and supraclavicular lymph nodes area. A total dose of 42.4 Gy divided in 16 sessions was applied. In addition, the patient completed 12 more courses of adjuvant trastuzumab 6 mg/kg. Posteriorly, the patient was followed up every 6 months with physical examination and an annual mammogram was performed.

In December 2019, the patient presented to the Emergency Unit of a private institution complaining of a 3-month history of worsening headaches and diminished sensation in the left facial area. A brain CT scan showed four intracranial lesions suggesting central nervous system relapse. Magnetic Resonance Imaging (MRI) defined a right temporal lobe lesion of 12 mm × 9 mm (Figure 1), a left temporal operculum lesion of 10 mm × 10 mm (Figure 2), a left parasagittal cingulum lesion of 12 mm × 11 mm (Figure 2) and left posterior parietal lobe lesion of 25 mm × 15 mm (Figure 3). In

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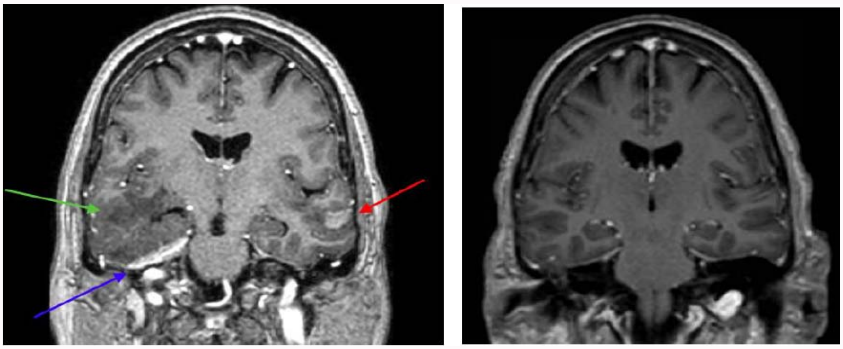

Figure 1: Left: T1 -potentiated MRI showing a left temporal operculum lesion (red arrow) and right temporal lobe edema (green arrow) both suggestive of metastasis. Leptomeningeal enlargement is also present suggesting leptomeningeal carcinomatosis (blue arrow) Right: Complete response.

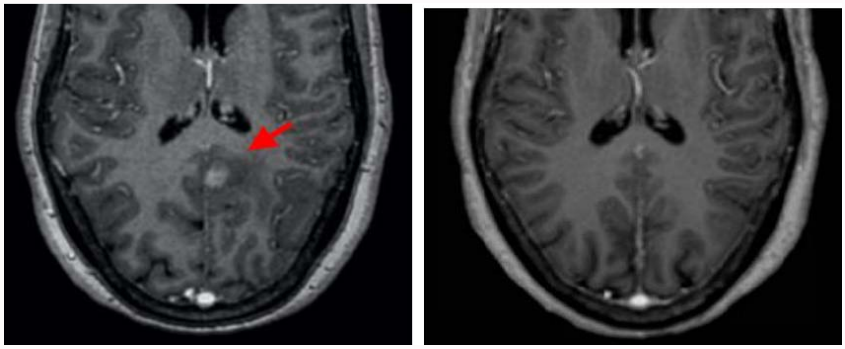

Figure 2: Left: T1-potentiated MRI showing a left parasagittal cingulum lesion suggestive of metastasis (red arrow). Right: Complete response.

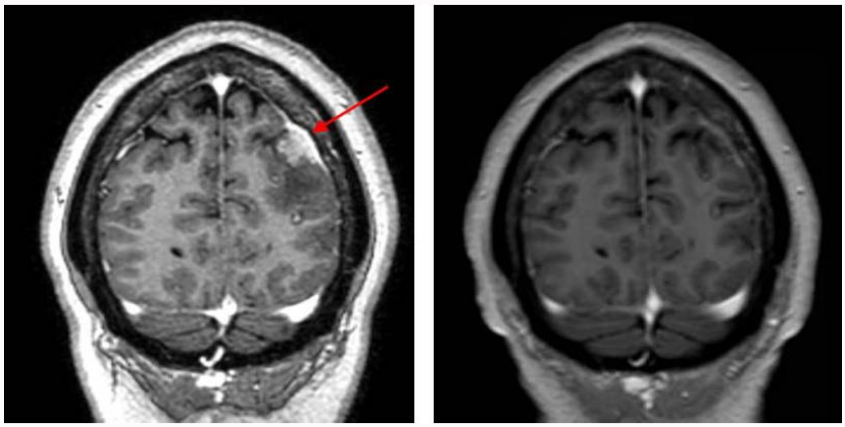

Figure 3: T1-potentiated MRI showing a left posterior parietal lobe lesion and edema suggestive of metastasis (red arrow). Right: Complete response.

addition, the MRI was suggestive of leptomeningeal carcinomatosis. A thoracic and abdominal CT scan excluded additional metastasis.

A first course of systemic therapy was started in December 2019 under the following scheme therapy: Pertuzumab 840 mg IV day 1 followed by 420 mg, trastuzumab 8 mg/kg IV on day 1 followed by 6 mg/kg IV cycled every 21 days and weekly paclitaxel 75 mg/m^2 IV. Clinical improvement was achieved after the first course of chemotherapy.

Subsequently, Whole Brain Radiotherapy (WBRT) was planned and the patient received a total dose of 30 Gy divided into 10 daily courses.

The patient seeked a second opinion in our Hospital in February 2020. The patient complained of headaches, although they have diminished in intensity and frequency since WBRT. Physical examination showed no neurological abnormalities. Performance status was 0.

After discussion, the same systemic therapy was resumed. Following completion of 8 courses of chemotherapy, the patient's symptoms completely solved and she denied any adverse events. MRI was performed in March 2020 and showed a complete radiological response-no lesions were present in neither the cerebral parenchyma nor the leptomeninges. A Positron Energy Tomography/Computed Tomography (PET/CT) scan was also performed and did not show any metabolic activity suggestive of metastasis.

The chemotherapy regimen was continued. In September 2020, after 9 months of treatment, a new PET/CT scan showed a maintained

complete response. After discussion, we decided to discontinue treatment balancing risks and benefits. A total of posteriorly, PET/CT and brain MRIs had been performed regularly every 6 months and the patient remains asymptomatic and maintains a complete radiological response at the time of submission of this paper-as for November 2021.

Discussion

Central nervous system is a common place of relapse of HER2 positive breast cancer. Trastuzumab based therapy has demonstrated to reduce recurrence rates, however CNS metastasis remains a sanctuary site for metastasis. Several clinical trials have evaluated the effectiveness of systemic therapies for brain metastasis, however patients with leptomeningeal disease were not included in such trials [1,2].

To our knowledge, this is the first reported case of a HER2 positive breast cancer with brain and leptomeningeal involvement that achieved a complete response after treatment with pertuzumab plus trastuzumab and docetaxel and maintained this response for 34 months.

The CLEOPATRA trial validated the use of pertuzumab in combination with trastuzumab and docetaxel for the first line treatment of HER2 positive metastatic breast cancer; however CNS metastasis was an exclusion criterion [3]. One phase II clinical trial evaluated CNS response in 25 patients treated with pertuzumab plus trastuzumab. Although CNS Overall Response Rate (ORR) was 12 %, accounting for four partial responses, no patient achieved a total response [4].

To date, the only phase III trial that proved increased overall survival in patients with untreated CNS involvement is the HER2CLIMB trial [5]. This trial randomized 291 patients with untreated brain metastases excluding leptomeningeal disease to receive tucatinib plus capecitabine plus trastuzumab versus capecitabine plus trastuzumab. Amongst all patients with brain metastasis, the tucatinib arm experienced improved overall survival (18 *vs.* 12 months, HR=0.58, 95% CI 0.40-0.85) [5] and improved overall response rate (47% *vs.* 20%, p=0.03) [6]. Four patients achieved a complete response- three in the trial and one in the control group.

Other clinical trials and clinical reports have documented the effectiveness of other systemic therapies including trastuzumab-emtansine [7], lapatinib plus capecitabine [8] and fam-trastuzumab deruxtecan [9]. However, patients with leptomeningeal disease were excluded from such trials.

There are some publications of case reports of patients with leptomeningeal disease responding to systemic anticancer therapies for HER2 positive breast cancer. For instance, a published case of a patient treated with intrathecal trastuzumab maintained a complete response for at least 31 months [10]. Nevertheless, this is the first case ever reported of a complete leptomeningeal response following treatment with trastuzumab pertuzumab and taxanes.

In spite that this is a unique case for the literature, we acknowledge that we lack an imaging study after WBRT and before systemic therapy. Therefore, although we believe that this patient responded to the combination of pertuzumab plus pertuzumab plus docetaxel, WBRT may have contributed in some degree to the achievement of this complete response.

Conclusion

This case constitutes the first report of a leptomeningeal and brain complete response following treatment with pertuzumab plus trastuzumab and paclitaxel. Additional case reports, case series and clinical trials should validate the effectiveness of this regimen for such disease locations.

References

1. Kuksis M, Gao Y, Tran W, Hoey C, Kiss A, Komorowski AS, et al. The incidence of brain metastases among patients with metastatic breast cancer: A systematic review and meta-analysis. Neuro Oncol. 2021;23(6):894-904.
2. Lin NU, Winer EP. Brain metastases: The HER2 paradigm. Clin Cancer Res. 2007;13(6):1648-55.
3. Swain SM, Baselga J, Kim SB, Jungsil R, Vladimir S, Mario C, et al. Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. N Engl J Med. 2015;372(8):724-34.
4. Lin NU, Pegram M, Sahebjam S, Ibrahim N, Fung A, Cheng A, et al. pertuzumab plus high-dose trastuzumab in patients with progressive brain metastases and HER2-positive metastatic breast cancer: Primary analysis of a phase II study. J Clin Oncol. 2021;39(24):2667-75.
5. Murthy RK, Loi S, Okines A, Paplomata E, Hamilton E, Hurvitz SA, et al. Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. N Engl J Med. 2020;382(7):597-609.
6. Lin NU, Borges V, Anders C, Hamilton E, Murthy RK, Paplomata E, et al. Intracranial efficacy and survival with tucatinib plus trastuzumab and capecitabine for previously treated HER2-positive breast cancer with brain metastases in the HER2CLIMB trial. J Clin Oncol. 2020;38(23):2610-9.
7. Krop IE, Lin NU, Blackwell K, Guardino E, Huober J, Lu M, et al. Trastuzumab emtansine (T-DM1) versus lapatinib plus capecitabine in patients with HER2-positive metastatic breast cancer and central nervous system metastases: A retrospective, exploratory analysis in EMILIA. Ann Oncol. 2015;26(1):113-9.
8. Bachelot T, Romieu G, Campone M, Diéras V, Cropet C, Dalenc F, et al. Lapatinib plus capecitabine in patients with previously untreated brain metastases from HER2-positive metastatic breast cancer (LANDSCAPE): A single-group phase 2 study. Lancet Oncol. 2013;14(1):64-71.
9. Modi S, Saura C, Yamashita T, Park YH, Kim SB, Tamura K, et al. Trastuzumab deruxtecan in previously treated HER2-positive breast cancer. N Engl J Med. 2020;382(7):610-21.
10. García FJV, Carrión NP, de la Cruz-Merino L. Long-term complete response to intrathecal trastuzumab in a patient with leptomeningeal carcinomatosis due to HER2- overexpressing breast cancer: Case report. Medicine (Baltimore). 2020;99(1):e18298.